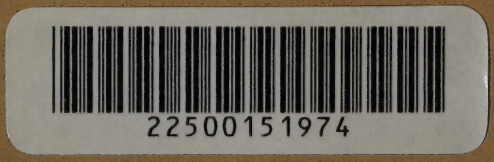
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PUBLIC HEALTH.

REPORTS

OF

THE MEDICAL OFFICER OF THE PRIVY COUNCIL AND LOCAL GOVERNMENT BOARD.

NEW SERIES, No. V.

PAPERS, CONCERNING THE EUROPEAN RELATIONS OF ASIATIC CHOLERA, SUBMITTED TO THE LOCAL GOVERNMENT BOARD IN SUPPLEMENT TO THE ANNUAL REPORT OF THE PRESENT YEAR.

Presented to both Houses of Parliament by Command of Her Majesty.

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No.

To the Right Honorable George Sclater-Booth, M.P.,
President of the Local Government Board.

Sir,

Medical Officer's Report.

In supplement to my recent Annual Report, I have now the honour of submitting to you (App. No. 1) the paper which I mentioned in that Report as at the time under preparation by Mr. Netten Radcliffe: setting forth the results of his laborious and instructive study of the international relations of Asiatic Cholera during the past ten years.

During that space of time, Asiatic Cholera made great ravages in other quarters of the globe than Asia; and especially as regarded our own quarter, the epidemic inroads of the disease were such that twice in the decennium the several European Governments consulted together in congress as to the possibility of better defending their States against a danger which seemed of growing importance. Of the two International Conferences to which I refer, one, lasting for more than seven months, was held at Constantinople in 1866; and the other, lasting for a month, was held last year at Vienna. The former was convened at the instance of the French Government with reference to the great pestilential invasion which in 1865 had radiated from Alexandria to all parts of Europe; the latter was convened at the instance of the Austro-Hungarian Government, with reference to the state of cholera in Europe during the years 1870–4. For an account of the more elaborate proceedings of the conference of 1866 I can only refer to the two valuable volumes in which the *Procès Verbaux* (including the reports of the Committees) of that Conference were published. For a full account of the proceedings of the second Conference, it is of course also necessary to refer to the published volume of *Procès Verbaux;* but, for more convenient reference on the present occasion, Dr. Seaton, who, with Dr. Dickson of Constantinople, attended the Conference on behalf of Her Majesty's Government, has, at my request, favoured me with the annexed brief abstract of the proceedings.—See App. No. 2.

Recent facts as to cholera in Europe have undoubtedly been of very evil omen. Europe, within the ten years' time, has twice been over-run with cholera. From the middle of 1865, when one great diffusion of the disease began, till after the middle of 1874, when a second great diffusion had apparently run its course, there possibly was no moment at which the disease was extinct in Europe, and there certainly was but little time when it could even be supposed to be extinct. It is true that, just at the end of 1868 and beginning of 1869, if traces were still remaining of the great diffusion which began in 1865, they were no longer publicly identified as such; but then, in the summer of 1869, began the second great diffusion, which was destined to have a five years' course. Whether or not there was latent continuity of process between those two great diffusions of cholera —whether the second of them began (as the phrase goes) in

"re-crudescence" of the first, or arose independently of it in a second invasive influence from Asia, has been matter of doubt among epidemiologists, and must perhaps remain undecided. Be that, however, as it may, the broad fact, concerning the nations of Europe, was that during the decennium 1865–74 Asiatic Cholera hardly ever ceased to more or less afflict or alarm them; and this fact, which, when duly understood, could not but suggest grave considerations as to the future, is receiving at the present moment a confirmation of its serious import in the circumstance that already, though only in the middle of 1875, cholera is reported to be again diffusing itself on the Syrian side of the Mediterranean.

Mr. Radcliffe's annexed paper is essentially narrative: telling facts which need no argument to emphasise their meaning; and, in submitting it to you, I would only beg leave to preface it with such few remarks as may help to define its practical bearings.

The special aim of the paper is to exhibit, with as precise detail as possible in regard of times and places, the various relations of cholera for the past ten years in this Western division of the Eastern Hemisphere: to show, as far as can be learnt, what local epidemics composed the total of each great diffusion; and in what order of time, and in what (if any) mutual connexion, they occurred; and in what (if any) way the local events were related to the circumstances of inter-local traffic. As regards the critical events of 1865, my annual report made to the Lords of the Council in 1866 had appended to it an excellent account then furnished by Mr. Radcliffe of such facts as were yet known; and the facts were likewise to some extent recorded by the Constantinople Conference of 1866; but, even as regards the events of 1865, Mr. Radcliffe is now able to add very materially to the knowledge which was possessed in 1866; and as regards all events subsequent to 1865, the evidence is now put together for the first time in Mr. Radcliffe's annexed paper.

The labour and difficulty of compiling such a record as Mr. Radcliffe has made are infinitely greater than persons who have never tried the same sort of work can well imagine. His raw material (consisting of all information received by different Departments of Her Majesty's Government with regard to the movements of cholera in foreign parts) has been of really immense quantity, but, though of such extent, has been often at first far too vague for scientific use, and has often failed to give essential facts; so that, before exact history could in any way be founded on the first material, much collateral inquiry has had to be undertaken; and occasionally long periods of time, even in some cases years, have elapsed before Mr. Radcliffe could succeed in getting certain links of evidence which were necessary to complete his record. Partly for this reason, and therefore unavoidably, Mr. Radcliffe's account of the second of the two great diffusions of cholera is far less elaborate than of the first; but, as a further reason for this difference, I may add that, when the one diffusion had been so exhaustively studied—studied

with a completeness perhaps never before attempted in regard of so large a passage of epidemiology, an equally detailed study of the other diffusion might, comparatively speaking, be dispensed with.

The practical results of Mr. Radcliffe's research are to be looked for in two directions: first, in the facts which are brought to light with regard to the influence of human intercourse in determining the diffusion of cholera; and secondly, in the inferences which arise with regard to the virtual illimitability of that influence (as between Asia and Europe) by measures of the nature of quarantine.

As regards the first matter, the evidence which Mr. Radcliffe exhibits is uniformly to one effect. So far as the extension of the disease could be followed in detail, it was found to have had definite relation to personal traffic: in various important cases the arrival of persons affected with the disease was unquestionably the starting point of local and perhaps national epidemics; and no extension of the disease was to be found, where the arrival of human beings from previously infected places was not either proven or probable.

It is important to appreciate those results in their negative as well as in their positive bearing. Detailed observation of particular outbreaks of cholera, and suggestions of analogy and experiment, have long led European pathologists to believe that the disease possesses great, though peculiar, power of spreading from the sick to the healthy; and Mr. Radcliffe, so far as he shews that particular cholera-epidemics have been started by imported cases of the disease, furnishes only additional illustration of that now (as I believe) unquestionable doctrine. But Mr. Radcliffe's other and merely negative result is in my opinion not less important: the result, namely, that in his very wide epidemiological study, extending from our own shores to the torrid climates of Africa and South-western Asia, he finds no reason to impute to cholera (outside the limits of India) any other mode of origination and extension than such as that doctrine expresses.

If, then, human contagion is the one active power in the international spread of cholera, is it possible so to restrict the intercourse between infected and non-infected countries as to prevent the spread of the contagion? Mr. Radcliffe's results, so far as I have quoted them, are eminently of a sort to suggest that question; but the impossibility of its being affirmatively answered was perhaps never so well illustrated as it is in parts of his paper.

In my above-quoted 8th Annual Report to the Lords of the Council, I entered at some length on the question, whether quarantine established at the ports of this country could be available to protect us against cholera: and I expressed a confident opinion that it could not. I submitted that quarantine, of a sort to be trusted in as a national defence, is not conceivable except in proportion as a people lives apart from the great highways of commerce, or is ready and able to treat its commerce as a subordinate political interest: that though undoubtedly quarantine, planned with the precision of a scientific experiment, and conducted with extreme rigour, may keep cholera out of places (such as remote and secluded islands) where the

extremely difficult conditions can be completely fulfilled, yet, under other circumstances, quarantine cannot reasonably be expected so to succeed, and must then be regarded as a mere irrational derangement of commerce. I presumed of course that our local authorities would individually have at command against the chances of cholera-importation the same powers of interference as against any dangerous infections of our own country, and that port-authorities might learn to exercise those powers in regard of evident arrivals of cholera in a way to confer at least some local service; but it seemed to me that, in the case of the United Kingdom, more than this could not be hoped for.*

That argument, primarily meant to apply to this country, might be expected to apply to other countries in proportion as they are commercial, or in proportion as great movements of population are kept up by other causes, as for instance in religious pilgrimages; and there are plenty of facts in Mr. Radcliffe's paper, to show how utterly futile against cholera were the quarantine-establishments of Europe in 1865. Egypt, aware early in May that illness of some sort was epidemic among the multitude of pilgrims then at Mecca, had provided that no returning pilgrims should disembark at Suez till their ships had undergone medical examination, and been found free from infectious disease; but during the latter half of May, ship after ship, bearing thousands of pilgrims, arrived at Suez without betraying any such evidence of disease as the authorities were prepared to consider a reason for quarantine; and Alexandria (as well as other parts of Egypt) received abundant choleraic infection from these arrivals, before any single case of cholera had been identified by the health-sentinels at Suez. Next, before Alexandria confessed itself to be infected, it had infected Marseilles; and through Marseilles it infected the rest of

* "In order to illustrate this view [as I argued in the above-quoted report] the medical postulates of quarantine deserve to be considered in detail. Quarantine, purporting to be effectual, cannot rest satisfied with excluding from entry such persons as are obviously sick, but, indispensably for its purpose, must also refuse to admit the healthy, till they shall have passed in perfectly non-infectious circumstances at least as many days of probation as the disease can have days of incubation or latency: this condition often involving as its consequence that, if one case of disease arise among a number of persons in quarantine, the whole number of apparently-healthy must recommence their period of probation, and this perhaps again and again. Now, setting aside, as not essential to quarantine, the cruelties which its mal-administration involves, and which in practice are almost identified with its exercise: criticising only the conditions which quarantine, if it is to be effective, must involve: and, for the moment, not even counting as an objection the cost of that gigantic establishment which has to be permanently maintained in order to meet occasional exigencies, I here insist only upon the restrictions. Considering what they, when really carried into effect, must involve—what inconvenience to persons, what interruption to commerce, and on how vast a scale, and for what indefinite duration of time, no one can expect, in regard of great trading communities, that governments, if they go so far as to enact, will have much success in enforcing, quarantine. Against the efficiency of it, when enacted, there operate some of the strongest of all law-breaking influences; on the one hand, instincts of contempt for the narrow self-protectiveness which it represents, and, on the other, those eager commercial interests which now mainly govern the world. The latter, in proportion as they are affected, elude the restrictions which would embarrass them. Contraband of quarantine, like ordinary smuggling, is developed as soon as the inducements for it are considerable. And thus, practically speaking, where great commercial countries are concerned, it can scarcely be dreamt that quarantine-restrictions will be anything better than elaborate illustrations of leakiness."—8th Annual Report, page 41.

France. Then, before Marseilles confessed itself infected, Valencia had received a most disastrous infection from or through it; and from Valencia all Spain was infected. Odessa, before it was recognized as itself having cases of cholera, had let infection pass through it, first to start in Podolia an epidemic which diffused widely in South Russia, and secondly to start at Altenburg in the middle of Germany an epidemic which diffused widely in Central Europe. Italy received its infection through the quarantine-establishment of Ancona; which both infected the town of Ancona by sending infected things to be washed there, and also allowed an undiscovered case of cholera to pass on from its lazaret, after six days detention, to infect the town of Pistoia.

The above cases, which were before the Constantinople Conference, could give little encouragement to a belief that, when cholera is once current in Europe, the individual States can protect themselves against it by respectively quarantining each other; and accordingly the Constantinople Conference, though it approved the continuance of such quarantines, insisted far more on the very important advantages which would be gained to Europe at large if the States, acting collectively, would establish at the mouth of the Red Sea a joint quarantine against Asia. At the Vienna Conference, where, as Dr. Seaton's annexed abstract sets forth, the resolutions of the Constantinople Conference were more or less re-considered, that recommendation for a joint quarantine at Babelmandeb was not expressly renewed, and was not, Dr. Seaton says, meant for renewal, but it was not expressly renounced; and as the Conference clearly adhered in principle to the recommendation of strict cholera-quarantine against Asia, I would observe that Mr. Radcliffe contributes material of particular interest with reference to the proposal of 1866. The proposal started from a belief that the infection of 1865 had come into the Red Sea as a direct importation from the far East; but Mr. Radcliffe gives facts which I think are conclusive against the correctness of any such opinion. He shows that before the arrival at Jeddah of the particular ships which the Conference believed to have infected the Hedjaz, and thus to have started the great outbreak of 1865, cholera had for some time been extensively prevailing both in the Yemen and Hadramaut provinces of southern Arabia and also in the Somali country on the African side of the Gulf of Aden; that the ships in question, instead of having brought cholera from farther east, had probably contracted it at Makallah; but that at any rate quarantine at the mouth of the Red Sea would, if it had existed, have dealt only with one of the dangers of infection to which the Hedjaz was at the time exposed; and further that, apart from the infection of the Hedjaz, cholera, early in 1865, was steadily making its way from Beloochistan up the Persian Gulf and Euphrates valley, to invade Europe otherwise than through Egypt.

I have noted that the facts which Mr. Radcliffe tells with regard to the spread of cholera in Europe in 1865 say little for the value of such cholera-quarantines as any one European State can maintain against any other; and the practice of this country in respect

of cholera in Europe has long recognised that little or no control can be exercised at ports of arrival except as to persons who on medical inspection are found manifestly infected with the disease. Control to this limited extent, not pretending to efficiency as a measure of national defence, but able to be of some local value where local authorities are vigilant in exercising it, and in principle scarcely exceeding that which is exercised in respect of small-pox or fever, is what this kingdom has in place of quarantine: and it is satisfactory to read in Dr. Seaton's abstract of the proceedings of 1874 at Vienna, as compared with those of 1866 at Constantinople, how strongly the balance of European opinion is now inclining to the side of our English practice.

As regards the interest which the world at large has in the preventability of Asiatic Cholera, Mr. Radcliffe's present paper does not pretend to deal with more than one section of a very great subject-matter; but he has so treated this section as to give additional importance to the sections which lie logically next to it; and the reader who would appreciate it in that connexion, should briefly pass them in review.

Cholera, as a geographical subject-matter, divides itself for our practical purposes into three sections: (1) cholera, as existing in India; (2) cholera, as diffusing to other countries; and (3) cholera, as we here, in England or generally in Europe, see it from time to time epidemic among us.

Persons regarding exclusively the second of those sections, and seeing it as now displayed by Mr. Radcliffe, might at first take an almost fatalistic view of the immense mischief which cholera inflicts on mankind. For they see the disease diffusing itself as an attribute of such vast social movements as it is evidently impossible to control or minutely scrutinize: spreading itself, namely, in all directions in those constantly-moving streams of religious pilgrimage and commercial enterprise which constitute very large proportions of national life: and they see that a first, but unattainable, condition of dealing completely with a contagion thus distributed would be that they should be able to immobilize at their discretion the great tides of human life which convey it. They would no doubt see that the marine exportation of cholera from India may be considerably impeded by an enlightened and vigorous supervision of shipping, such as Her Majesty's Indian Government have designed under the Acts (constantly in course of amendment) which relate to native passenger-ships; but they would fear that, even if only in such movements of land-population as comparatively escape control, means must continue by which cholera existing in India will have ample facilities for extending to Europe; and they would recognise how the progress of circumstances is constantly making it less and less possible that, at times when cholera is present in any territory of Europe, the other territories should succeed in really protecting themselves against it by restrictions on international movement.

Undoubtedly, therefore, it is in directions which are outside the view of Mr. Radcliffe's present paper, that we must mainly look for

such hopes as can be entertained of dealing effectively with this great pestilence. We have to hope, on the one hand, that India may be made less productive of the infection: we have to hope, on the other, that other countries may be made less susceptible of it. And in each of these directions, there is room for very hopeful work.

Of the conditions which in Europe make local susceptibility to the infection of cholera, I have often had occasion to speak. That cholera, when imported into a locality, will under certain circumstances spread from the sick as from a centre, is among the certainties of medicine; but we know with at least equal certainty that its means of thus spreading are strictly limited, and the limiting conditions which are best known to us in regard of it are those which bring it into intimate analogy with our own enteric fever, and justify us in classing it as a Filth-Disease. On the preventability of cholera in this point of view, I have said so much on other occasions that I need not now insist on it, and would only refer to the general report which I had the honour of laying before you a year ago, on the subject of Filth-Diseases and their Prevention.* It cannot I think reasonably be doubted but that, as conditions of filth, and especially as filthy conditions of water-supply, are the main facilitating conditions for the dissemination of cholera in Europe, so they must be immensely potent influences in favouring the advance of cholera from station to station in successive epidemic outbreaks in the countries which lie between India and Europe; and it would seem certain that, along the whole succession of lands which transmit the streams of westward traffic from India, common hygienic vigilance in respect of those conditions may be of very great effect in impeding the diffusion of cholera.

Regarding cholera in India, apparently two sets of conditions have to be distinguished: (a) the conditions of the disease's endemic prevalence, in larger or smaller quantity, in a limited portion of the Indian continent, and (b) the conditions of its occasional spread over areas indefinitely larger.

That under the latter head must be counted at least in part the same property of contagiousness, and the same relation of this property to circumstances of filth, as we knew to be the essential conditions for the extension of the disease in Europe, is an opinion which European pathologists find it impossible not to entertain:† and so far as that European opinion holds good, the amount of cholera-diffusion in India is likely to be controlled by the same preventive measures as are certainly effectual for the like purpose in Europe. Those parts of the world therefore, which have had the habit of receiving cholera-infection from India, and especially those which have received it from secondary centres of infection, may expect to incur less and less of this danger in proportion as common sanitary government shall more and more bring within control the

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* Report, New Series, No. II.

† If this opinion is less generally entertained in India, or in parts of India, than it is in Europe, probably the difference of opinion is in great part only an expression of the fact that it must be more and more difficult to prove the contagiousness of the disease in proportion as studies on this point are made in places where the disease may be autochthonic

common Filth-Diseases of that vast country. And in this point of view it is most hopeful to know that for many past years, and even more rapidly than Europe has been able to appreciate her own interest in the sanitary progress of India, the British Government has been organising in that part of the empire such provisions for sanitary government as promise soon to compare not unfavourably with the present institutions of Europe itself.

The distinctive Indian problem, however, is that of the endemicity of cholera in part of the Indian area. It is from within British territory that this enemy of the human race sallies forth from time to time to do world-wide execution; and the first threat of each coming foray is that the disease is produced in greater quantity in the area to which it primarily belongs. There, in lower Bengal—specially in the Sunderbunds and other alluvial lands from Juggernauth to beyond the mouth of the Bhurmpooter, cholera is said to be as normal to the district as ague to the marsh-lands of Europe, and as definitely related to the seasons as if it were a fruit of the earth. To learn the conditions of that endemicity and its variations is a problem of the highest science; and to control them in the interests of mankind will be among the noblest administrative tasks which the responsibilities of empire have ever imposed. It would be foreign to my province to dwell upon this part of the subject: but I may permit myself to advert to the fact that Her Majesty's Government, now for some years past, has been promoting the study of cholera in India with the best lights of contemporary European knowledge: and no one will doubt but that here, as in other departments of medical research, truly scientific study must eventuate in practical good.

Briefly then,—if the constantly-developing and constantly-accelerating commerce between India and the rest of the world is not to carry with it a constantly-increasing terror of pestilence, the safeguards, I apprehend, will consist, not in contrivances of the nature of quarantine to maintain from time to time more or less seclusion of nation from nation, but rather in such progressive sanitary improvements on both sides as will reduce to a minimum on the one side the conditions which originate the infection, and on the other side the conditions which extend it. That cholera, as endemic and epidemic in India, will, even in the near future, be rendered by the exertions of the British Government far less terrible to Europe than it has been for the last half-century, is a conclusion which I think cannot fail to be entertained by those European epidemiologists who are conversant with the annual volumes, printed by order of the Secretary of State for India in Council, with regard to the measures adopted for sanitary improvements in India.

I am, Sir,
Your obedient Servant,

JOHN SIMON.

Medical Department,
July 28, 1875.

APPENDIX,

No. 1.—Report by Mr. Netten Radcliffe on the Diffusion of Cholera, and its Prevalence in Europe, during the Ten Years 1865–74.

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Preliminary.

Europe had been free from Asiatic cholera barely four years,* after fourteen years' uninterrupted presence of the disease, when in the summer of 1865 a new invasion took place. This invasion differed from preceding invasions in the direction of its approach and in the rapidity of its progress. The great epidemics beginning in 1830 and in 1847 respectively, had invaded the continent by way of Caucasia and

* The disease, after its invasion of Europe in 1847, appears to have lingered longest in Russia, and according to Dr. Arkhangelsky, in his work on the Cholera Epidemics of European Russia, 1823–72 (St. Petersburg, 1874, p. 197), that country became quite free after 10th July 1861.

the Caspian Sea; and each occupied 15 months in traversing the continent and reaching this country. The epidemic beginning in 1852 was, primarily at least, a recrudescence of the preceding epidemic. The epidemic beginning in 1865 invaded the continent by way of Egypt and the Mediterranean Sea, and in less than five months from its appearance at Alexandria, it had attacked numerous places along the whole coast-line of southern and eastern Europe from Taganrog to Gibraltar, and had appeared at Southampton. It had penetrated also into the governments of Podolia and Kiev, in Russia, along the course of the Danube as high as Rustchuk, into the interior of European Turkey and of Piedmont, and to the suburbs of Paris.

Early in 1866, at the request of the Medical Officer, I prepared for the Lords of the Council a report on the sources and development of the invading cholera of 1865.* For the purpose of this report I was given access to the very important information received by the Foreign Office from Her Majesty's representatives in invaded districts, and communicated by the Secretary of State for Foreign Affairs to their Lordships. The report was chiefly successful in showing that no more mysterious agency was concerned in the rapid diffusion of the disease from Alexandria than steam navigation. All the sea-port towns earliest attacked were in direct communication with that city; and in every instance where the beginnings of the irruption had been investigated with any precision, there importation was obvious or so highly probable as to be well-nigh as certain. The report was less successful in showing the sources of the invading cholera, except in relation to Mecca and the pilgrimage there. An unusual number of pilgrims had gathered together at Mecca in 1865 in consequence of that year being a Mahommedan jubilee. The days set apart for the peculiar rites of the pilgrimage fell in the first week of May. During the performance of the rites cholera broke out among the assembled pilgrims with great destructiveness, and at the close of the pilgrimage the disease was carried by those pilgrims who returned homewards from Mecca by way of Jidda, the Red Sea, and Suez into Lower Egypt. The first of the returning pilgrims, 1,500 in number, crowded on board an English steam vessel, arrived off Suez on the 19th May 1865. They were disembarked on that or the following day, and with them cholera was also disembarked, carried ashore by, among others, the master of the vessel and his wife, both of whom sickened of the disease in Suez on the 21st May.

From Mecca to Suez the manner of diffusion of the malady was pretty clearly ascertained; and its subsequent diffusion in Lower Egypt and to Europe could be followed step by step. But the source from which Mecca became infected with cholera, and the original starting point of the diffusion were less apparent, and this part of my report I left confessedly imperfect. The undetermined questions here referred to, of much interest epidemiologically, became of considerable practical importance in the course of the proceedings of the International Sanitary Conference held at Constantinople in 1866. The Conference came to the conclusion that cholera had been introduced into the Hejaz in 1865, from Java and India (more accurately, according to its report, from Bengal), by pilgrim-carrying ships; and upon this conclusion they founded certain recommendations for diminishing the danger from cholera, primarily to the Hejaz, and secondarily to Europe, by the

* Report on the Sources and Development of the present Diffusion of Cholera in Europe. *8th Report of the Medical Officer* (1865), p. 306.

establishment of a sanitary or, in other words, quarantine station at the mouth of the Red Sea. The Conference did not appear to have had before it evidence of the epidemic activity of cholera in the Bombay Presidency in 1864 and the beginning of 1865, which would have suggested greater significance than the Conference attached to information submitted to it by the British medical delegates, Dr. E. D. Dickson and Dr. Goodeve, as to the probable existence of cholera in Yemen at the close of 1864. Neither does it appear to have had any suspicion of the existence of cholera in the Somali country and East Africa, prior to the appearance of the disease in the Hejaz. The facts stated in my report were sufficient to prove that the conclusion of the Conference of 1866, and the recommendation attached to it, should not be received without further inquiry ; but if it were to be understood (which Dr. Seaton informs me is not the case) that the International Sanitary Conference which met at Vienna in 1874, accepted (as the words of one of their resolutions might seem to imply) the recommendation of the Conference of 1866, regarding a sanitary establishment at the mouth of the Red Sea, this would show that the information which has been accumulated on this subject is still very imperfectly appreciated.

The knowledge which was available concerning cholera in East Africa when my report was written was of the most meagre description. I was long foiled in obtaining confirmation of the suspicion, expressed in that report, of the disease existing there early in 1865. It was not, indeed, until 1870, that I was enabled to obtain specific information on the subject. In that year an opportunity offered of asking assistance from the Right Reverend Bishop Tozer, of the Universities Central African Mission, and he very courteously gave me the invaluable help of inducing Dr. James Christie, the physician to the Sultan of Zanzibar, to give attention to the question which had foiled me. Dr. Christie, with infinite care and much local knowledge of places, languages, and persons, elicited the positive fact of prevalence of cholera in the Somali country early in 1865. Taking, moreover, a wider interest in the subject (stimulated no doubt by the terrible epidemic of cholera which had visited the Island of Zanzibar in 1869–70), he collected from native and other sources all accessible information regarding the different diffusions of cholera to which East Africa had been subject. This information, of peculiar epidemiological interest, and forming a wholly new chapter in the history of cholera, was communicated by Dr. Christie to the Epidemiological Society, partly in January 1871 and partly in February 1872,* and is published in detail in the Transactions of the Society. The movements of cholera in East Africa form a most instructive study with reference to the mode in which the disease is propagated from place to place, and Dr. Christie is still engaged in researches on this subject.†

The presence of cholera in the Somali country early in 1865 materially alters the question of the origin of that year's diffusion, as it was presented to the International Sanitary Conference of 1866, and imparts peculiar importance to the opinions of the British medical delegates, that cholera probably existed in Yemen at the close of 1864. The infection of the Hejaz in 1865, was subsequent to the infection of the Somali country. Both phenomena were obviously parts of the same

* *Transactions of the Epidemiological Society of London.* Vol. III. pt. 2, pp. 265–287.

† Dr. Christie has completed his researches, for the present, since this report was written and he has published them as an independent work entitled "*Cholera Epidemics in East Africa : an account of the several diffusions of the disease in that country from* 1821 *till* 1872." (London, 1876.)

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principal diffusion, but the explanation adopted by the Conference as to the sources from which the Hejaz received infection is inadequate to explain the source from which the Somali country received it.

Preliminary.

It is now practicable to treat with some approach to accuracy the question of origin of that great diffusion of cholera which, so far as Europe is concerned, began in 1865; and it is important from the prominence which this question has received in recent efforts to promote measures of international hygiene, as also from its epidemiological interest, that it should receive full consideration.

My report in 1866 was necessarily limited, almost wholly, in addition to such facts as were then available regarding the origin of the outbreak of cholera in Mecca in the preceding year, to an account of the subsequent spread of the disease in the Levant and in Europe. Such account represents very imperfectly the influence of the pilgrimage of 1865 in the dissemination of cholera, and the importance of Mecca as a centre of epidemic diffusion, when great outbreaks of epidemic disease there concur with the pilgrimage. This early report requires to be supplemented by the additional information which has been obtained on the subject to which it refers since its publication.

In the present report I propose to set forth the facts now ascertained concerning the sources of the outbreak in Mecca in 1865, and discuss their significance; also to describe the diffusion of the disease along the various routes pursued by the pilgrims on their homeward return after the close of the pilgrimage. I propose, moreover, to indicate the progress of the epidemic in Europe subsequently to 1865, and to offer some observations on its recurrence in 1869–70. I have in view to bring together so much of the official information communicated to this Department, during the course of the epidemic, as may serve to throw additional light upon certain questions not adequately treated in published reports. I have no purpose of writing an exhaustive history of the epidemic. The reports which have been published in reference to the prevalence of the disease in several Continental States and in America, official and other, are very numerous. The more important of these are readily accessible, and I have no pretension to that command of languages which would be requisite for the digestion of the entire series, even if such digestion were consistent with my present object. There are, however, certain important questions relating to the epidemic which, as I have already intimated, may be elucidated by official information communicated to this Department, and it is to these questions, and to such other additional knowledge on the subject of the epidemic as may be gathered from official papers, that I devote this report, supplementing the official data with data derived from other sources only so far as may contribute to greater clearness of the questions treated.*

Origin of the diffusion of 1865. The first observed facts.

I. The Origin of the Diffusion of 1865.†

On the 28th February 1865, the British ship "North Wind," a sailing vessel, over 60 days out from Singapore, arrived at Jidda with

* The data given in this Report relating to the Ottoman Dominions are for the most part derived from reports prepared at frequent intervals during the diffusion by Dr. E. D. Dickson, the physician to Her Majesty's Embassy, Constantinople, and British delegate to the Ottoman General Board of Health. Dr. Dickson's long acquaintance with and large knowledge of Turkey, give to the data furnished by him quite an exceptional value. At the International Sanitary Conferences held respectively, the one in Constantinople in 1866, the other in Vienna in 1874, Dr. Dickson was one of the British representatives.

† In dealing with geographical proper names in this Report, I have chiefly followed the orthography of Keith Johnston's *Index Geographicus* (1864).

numerous Javanese pilgrims on board bound for Mecca. She had left Singapore in December 1864 ("a few days later" than the 13th), and had touched in the course of her voyage at Malacca, Penang, Pedir, Achin, Aleppy, Shehr, and Makallah, putting into the last-named port on the 11th February 1865, and leaving it on the 14th.

On the 8th March another British ship, the "Persia," also a sailing vessel, 85 days out from Singapore, arrived at Jidda. She carried many pilgrims for Mecca, principally Javanese, and had left Singapore on the 13th December 1864. In her course she touched at Aleppy and Makallah, being about 20 days on the voyage between the two places. She reached Makallah on the 13th February 1865, and left that port for Jidda on the 16th.

Both ships were visited severely by cholera after touching at Makallah. While in that port a brackish water (the only water procurable) had been obtained for ship's use, and the passengers and crews had indulged immoderately in an unwholesome kind of fish sold there. The disease, favoured, as the masters believed, by a prevalence of calms and fair winds, which prevented the efficient ventilation of the between decks, continued until the ships arrived opposite to Lith (about 100 miles south of Jidda) and met with the strong northerly winds constantly blowing at that season in this part of the Red Sea, when it ceased. The master of the "North Wind" reported 52 deaths from cholera among a total number of 632 passengers and crew; the master of the "Persia" 93 deaths, among a total number of 530 passengers and crew.

Nothing is known of the early history of the outbreak on board the "North Wind," except that it began after the ship had touched at Makallah. Of the commencement of the outbreak on board the "Persia" there are two statements, both made twelve months after the occurrences described, one by the master of the vessel to Mr. Raby, Her Majesty's Consul, at Jidda; the other by an Arab passenger, who joined the ship at Makallah, to Dr. Hassan Effendi, the Egyptian sanitary agent at Jidda, in 1866. The master stated that two cases of cholera were observed on board on the third day after the ship put into Makallah. Dr. Hassan Effendi's informant stated that the disease manifested itself six or seven days after the departure from Makallah. These statements may not in reality be inconsistent with each other, as the cases referred to by the master may have happened while the ship was still in port, and before Dr. Hassan Effendi's informant went on board, while the cases to which the latter refers may have been the earliest of the subsequent development of the disease.

Probable presence of Cholera in Hadramaut early in 1865.

Dr. Hassan Effendi's informant, with about 70 pilgrims, all from Hadramaut, took passage for Jidda, by the "Persia," from Makallah. He joined the ship two days after his arrival at Makallah from the interior. The persons first attacked with cholera on board under his observation were, he said, passengers from Makallah; and he added that two months after his arrival at Jidda he had received a letter from his family in Hadramaut in which it was stated that cholera prevailed in their district, and had caused the death, among others, of one of his aunts.*

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* The following is Dr. Hassan Effendi's statement, read at the meeting of the Council of the General Sanitary Intendance of Egypt, 30th May 1866:—

"L'Intendance Sanitaire m'ayant confié le service sanitaire, je me suis appliqué à remonter à la source du choléra de l'an dernier. En faisant la visite réglementaire à bord du navire nommé *Tarsia* [*Persia*], provenant de Singapor, une occasion propice à mes recherches s'est présentée; car il m'avait été dit que ce navire

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The foregoing are the ascertained facts respecting the earliest known appearances of cholera on the Hadramaut coast and in the Red Sea in 1865. Another sailing ship from Singapore, the "Ruby," bound for Jidda, and carrying 500 pilgrims, was also attacked by cholera after touching at Makallah, and had 90 deaths from the disease on board. Other ships, moreover, carrying pilgrims from Bengal, *e.g.*, the "Meris Merchan" and the "Boy-Meyr," had fatal cases of cholera and diarrhœa on board. No account of these vessels has been furnished to the Department other than what appears in the proceedings of the International Sanitary Conference, 1866,* and this does not give the dates of sailing from the ports of departure nor the dates of arrival at Jidda, nor, except in the case of the "Ruby," the period of voyage at which fatal cases of cholera and diarrhœa occurred.

While the events just related were taking place on the north coast of the Gulf of Aden, events were happening on the south coast of the gulf a knowledge of which is necessary to a right interpretation of the former.

Cholera on East African coast and in Somali-Land at beginning of 1865.

In April 1865, at the commencement of the south-west monsoon, cholera made its appearance in the districts adjacent to the mouth of the river Jub. The disease subsequently extended down the coast as low as Mombassa, attacking severely Patta, Lamoo, and Melinda, when its progress

était précisement celui qui, l'an dernier, avait eu la maladie à bord. Je me disposais à procéder à un interrogatoire en règle, mais il ne se trouvait à bord ni le capitaine, lequel était marin en ce moment à Suez, ni aucun des marins qui avaient fait le voyage l'an dernier. Néanmoins mes recherches obtinrent du succes, car je découvrais un parent du propriétaire du navire (un nommé Ahmat Bascaraïl), et ce parent était le seul de ceux qui avaient fait le voyage avec le navire en question.

"Je me rendis donc auprès de la personne susindiquée, et la priais de me raconter les circonstances du voyage en question. Voici à peu près ce qu'elle m'a raconté :—

"Étant retourné l'an dernier de Kadramat [Hadramaut], et étant arrivé à Makalla, un des ports du golfe Persique, j'y trouvai le navire *Tarsia* [*Persia*], et je pris passage sur ce navire avec environ soixant-dix pélerins venant de Kadramat. Deux jours après mon arrivée à Makalla, c'est-à-dire le 18 Ramadan 1281 [12th February 1865], je me rendis à bord du navire où j'avais retenu ma place, et j'y trouvai environ quatre cents pélerins arrivés de Singapor, et le navire ainsi chargé parvint jusqu'a Gebel El Fuir, localité voisine d'Aden.

"Six ou sept jours après notre départ de Makalla une maladie se déclara à bord ; c'étaient des coliques, des crampes, de grandes froids aux extremités du corps, vomissements, diarrhées. Chaque jour cette maladie enlevait quatre ou cinq personnes, dont le décès avait lieu douze ou quatorze heures seulement après l'attaque. Nous eûmes, tout compte fait, environ cinquante décès en neuf jours. Lorsque nous arrivâmes à Djeddah, le 6 Chawal [6 Shawâl, 2nd March 1865], il y avait déjà trois jours qu'il n'y avait pas eu de décès a bord, et de Djeddah les passagers partirent de suite pour la Mecque.

"On doit croire, d'après les symptômes décrits ci-dessus que la maladie en question était le choléra. Je demandais ensuite dans quelle catégorie de pélerins la maladie avait debuté, et il me fut répondu que c'etait parmis ceux de Makalla. Deux mois après, continua la personne interrogée, je reçus une lettre de mes parents de Kadramat, dans laquelle lettre ils me racontaient que la maladie, *le vent jaune*,[1] faisait des ravages dans mon pays, et qu'elle avait même enlevé une de mes tantes." (*Procès-Verbaux des Séances du Conseil de L'Intendance Générale Sanitaire d'Egypte, présidé par M. le Dr. Colucci Bey depuis l'Apparation du Choléra en Egypte en* 1866, *jusqu'a sa cessation en* 1865. *Paris*, 1866, *p.* 145.)

* See *Rapport sur la Marche et la Mode de Propagation du Choléra.* (Annexé au Procès-Verbal, No. 23), p. 3. Also Fauvel, *Le Choléra, Etiologie et Propalaxié.* Paris 1868, p. 248.

[1 "Rih el Asfar ; properly meaning the yellow wind or air, or Cholera Morbus." Burton. *Personal Narrative of a Pilgrimage to El-Medinah and Mecca.* Vol. II., p. 174 and note.]

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southwards is stated to have stopped contemporaneously with the stoppage of the southern coasting traffic on the setting in of the south-west monsoon. In Patta and Lamoo cholera prevailed until June, and in other infected localities on the coast it lingered until August. Dr. Christie, seeking for the origin of this diffusion along the African coast, ascertained from residents at Mukdisha (Magadoxa) that the disease had reached that town from the south, having previously been prevalent in Brava and Merka. The further investigation was worked out with the assistance of Mr. Brenner, one of the members of Baron Von der Decken's expedition, which, leaving Zanzibar in May 1865, when cholera was prevailing with great violence in the coast towns north of Mombassa, entered the River Jub in June, and proceeded along its course as high as Barderah. The expedition did not escape from the disease, several natives attached to it dying from cholera, and the Baron himself suffering a violent attack. On reaching Barderah, where shortly afterwards the Baron and the medical officer of the expedition were brutally murdered, it was found that cholera had been prevalent there a short time before, but had then ceased, and on inquiry from what source the malady had reached Barderah, information was received that it had previously prevailed at Gananah and Berbera. Cholera, in fact, according to this information, had first shown itself at Berbera, on the south coast of the Gulf of Aden, during the annual fair there, and had travelled southwards with returning traders along the ordinary caravan route to Gananah and Barderah. From Barderah the disease had passed to the mouth of the Jub and to Brava, and afterwards spread north and south along the coast.

The significance of the facts related in my previous report, from which I inferred the probable presence of cholera on the East African coast early in 1865, can now be understood. These facts were as follows :—On the 15th April 1865, Her Majesty's ship "Penguin," cruising off the east coast of Africa, captured near Mukdisha a dhow, running northwards with the south-west monsoon, and containing 127 slaves. While conveying the dhow to Aden, a considerable number of the slaves died from choleraic malady, which prevailed among them. One of the crew of the "Penguin" was attacked with a similar malady on the 17th April, and died after twenty hours illness. The same ship, it may be added, while cruising further north in the passage leading between Cape Guardafui and Socrata, captured another dhow, laden with 160 slaves, on the 16th May 1865. These slaves also suffered during the voyage to Aden, to which port the dhow was taken, from the same kind of choleraic malady as had been observed among the slaves in the dhow captured on the 15th April, and many died. On the 16th May, four days after the capture of the second dhow, another of the crew of the "Penguin" had a choleraic seizure, and died after eight hours' illness. Assistant-Surgeon George Maclean, reporting these occurrences at the time, observed, "In both cases the general symptoms were precisely similar to those of epidemic cholera."† There cannot well be a doubt, having regard to the knowledge now obtained of the existence of cholera in the Somali country and on the east coast of Africa north of Mombassa at the time of the captures, that the fatal affection among the slaves, and which carried off two of the crew of the "Penguin," was cholera. Cholera, it may be mentioned here, broke out in the town of Aden on the 22nd May 1865, and among the European troops stationed there on the 25th. The disease spread from the peninsula into the adjacent districts of Lahej and Foudeli.

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* *See* Mr. Maclean's account of the symptoms in the *Statistical Report on the Health of the Navy for* 1865, p. 240. I was indebted, in the first instance, to Deputy-Inspector General Dr. Mackay, the Medical Officer at the Admiralty, for a knowledge of the events related in the text concerning the "Penguin."

Dr. Christie has satisfied himself that the history, given above, of the progress of cholera across the Somali country, from Berbera to the East Coast, early in 1865, is substantially accurate. The fair at Berbera, which is largely frequented by native traders from the interior and from Southern Arabia, and the coasts of the Persian Gulf and West Hindostan, begins in October or at the commencement of November, and ends late in April or early in March. In the interval the place is deserted. At the ordinary rate of travel pursued by native caravans, three months at least would be occupied in a journey from Berbera to the East Coast, by way of Gananah and Barderah. Hence Dr. Christie concludes that in order to account for the appearance of cholera on the East Coast, by extension along this route, at the period the disease was first heard of on the coast in April 1865, it must be assumed that an infected caravan left Berbera for Gananah and Bardera not later than December 1864. In other words, Dr. Christie believes, that cholera was present in Berbera before the close of that year, and most probably in the month of November; if, indeed, it were not introduced there and carried into the Ugahden district at the close of the fair of 1863–64.

No information appears to have been received by the Political Resident at Aden respecting Berbera during the fair-season of 1864–65; but in his official report for the period he refers to the fair as having been "broken up." I am unable to reconcile this statement with information as to the fair, derived from native sources on the East African Coast; and with Sir Bartle Frere's reference to the fair in the correspondence respecting his Mission to the East Coast of Africa in 1872–73.* In a despatch dated the 29th May 1873, he writes of the "annual commercial fair" at Berbera, and of its importance with regard to the subject of his Mission, and makes no allusion to any alteration in its character or to its decline as a native mart. He supplies, moreover, an explanation of the little knowledge possessed of Berbera, at the period under consideration, by the British representative at Aden, by referring to the "jealously-guarded system of non-intercourse" with the Somalis and their country, which was for many years "insisted on by the Indian authorities," and which has only latterly been relaxed.† It is noteworthy that the official report from Aden, which mentions the two dhows captured by the "Penguin," and brought into that port, makes no reference to the prevalence of choleraic disease among the slaves on board.

Before attempting to show the relationship existing between the different occurrences of cholera already recorded on the Hadramaut coast and in the Somali country early in 1865, it is necessary to state certain facts regarding other manifestations of the disease on the Arabian coast before the great outbreak at Mecca.

Probable cholera in Yemen in winter of 1864-5.

In the course of April 1865, cholera became prevalent in Hodeida, and it had appeared in several of the coast towns of the Hejaz, notably Confodah and Lith.

Assuming that the statement of Dr. Hassan Effendi's Hadramaut informant is substantially correct, it is to be inferred that cholera was prevailing in the interior of that province about the same time that it had become prevalent in Hodeida and elsewhere in Yemen.

It would appear, indeed, that cholera was actively prevalent in parts of Yemen, and probably also of Hadramaut, and that it was, moreover, prevalent in the Somali country and on certain parts of the East African coast in April 1865.

The question of origin of the different occurrences of cholera which have been described will perhaps best be considered, first, with reference

* Presented to Parliament, 1873. † See Correspondence, p. 145.

to the conclusion arrived at regarding the introduction of the disease into the Hejaz by the International Sanitary Conference of 1866.

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The Conference held that there were two sources from which cholera had been imported into the Hejaz in 1865, namely Java and India; and in respect to India the particular source of infection indicated in its proceedings was Bengal. According to information furnished to the Conference by the Consul General of the Netherlands at Singapore, cholera had been very prevalent in Java and in Singapore in 1864, and instances were known of persons sick of cholera and convalescent from the disease having embarked that year on ships bound for the Hejaz. Instances have been cited in a previous paragraph of fatal cholera and diarrhœa occurring on board ships sailing from Bengal ports for the Hejaz. The Conference expressed no opinion on the probable existence or not of cholera at Makallah previous to the arrival of the ships "North Wind" and "Persia" there; but its definitive conclusion as to the source of infection of the Hejaz, necessarily includes the source of infection of the three ships which were attacked with cholera after touching at Makallah.

THE STARTING POINT OF THE DIFFUSION.

Question of Importation from Singapore and Bengal.

The usual length of voyage for sailing vessels engaged in carrying pilgrims from Singapore, the common port of embarkation for Javanese pilgrims, to Jidda, is 50 days, and, as proved in the instance of the "Persia," it may exceed 80 days. The usual length of voyage for sailing vessels from Calcutta (the port of embarkation from which the majority of the Bengal pilgrims come) to Jidda is from 60 to 75 days. Vessels from Singapore, as a rule, touch at Makallah, vessels from Calcutta at Aden or Hodeida. The Conference appears to have assumed that a case of cholera, occurring at a given date, may be referred directly, without the intervention of any other case, to cholera which had existed 50 to 80 days previously. I am not aware of any facts that justify such an assumption. There is no evidence forthcoming of the continued prevalence or of the occurrence of cholera in the interval of voyage, on board any of the ships arriving off the Arabian coast from Singapore and Bengal; and the fact of having sailed from an infected locality cannot be admitted as sufficient to support an assumption of practically an indefinite retention of the infection of cholera by the passengers or their goods.

If ships arriving from Singapore and from Bengal were the carriers of infection to the Hejaz, in 1865, the source of their infection should be sought, not in the original port of departure, but in some intermediate port at which they touched in their voyage. All sailing vessels from the Strait Settlements and from Bengal, bound for the Hejaz, probably touch at one of the ports on the Malabar coast for water and supplies. Both the "North Wind" and the "Persia" touched at Aleppy. The last-named ship, as already stated, was about 20 days in her passage from Aleppy to Makallah; the first-named, judging from her more rapid voyage between Singapore and Makallah, and Makallah and Jidda, would be a shorter time in passage. These vessels were at Aleppy at the period of commencing activity of one of the severest visitations of cholera from which Malabar and the western coast districts of Southern India has suffered.

It has not been practicable to push investigation of the question beyond this point, and probability of infection of the vessels when at Aleppy must be inferred from the events which occurred after they had touched at Makallah. The appearance of cholera on three Singapore vessels after having touched at Makallah suggests, in the first place, their reception of the infection in that port. It is certainly not inconsistent, in the cases of the "North Wind" and "Persia," with the assumption that the disease might have been contracted on the Malabar coast, although the coincidence of delayed development until after

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Makallah had been reached would be remarkable. The information given by the masters of these vessels, immediately after their arrival at Jidda, to Mr. Henry H. Calvert, then Her Majesty's Acting Consul there, led him to the conclusion that cholera existed at Makallah when the two ships anchored in that port, and that they had been infected by the disease during their stay in it. This would appear to have been the belief of the masters at the time; but twelve months afterwards the master of the "Persia," when questioned on the subject by Mr. Raby, Mr. Calvert's successor in the consulate, stated that he had been informed at Makallah that no cholera existed there when his ship touched at the port in 1865. The statement made by Dr. Hassan Effendi's Hadramaut informant is consistent with the assumption either that the passengers from Makallah had contracted the disease before they went on board the "Persia," or, the disease previously existing in the ship, that they had received the infection after joining. If the former supposition be the most probable, assuming the freedom of Makallah from cholera at the time of arrival of the ships there, it would follow that pilgrims from the interior of Hadramaut, coming from the district in which, according to Dr. Hassan Effendi's informant, cholera had soon after his departure become prevalent, brought the disease with them into the town. On the other hand, assuming that one or both of the ships had imported the disease into Makallah, there may perhaps have been time, between the departure of Dr. Hassan Effendi's informant from his home and the manifestation of cholera there, for importation of the disease from Makallah. Or, indeed, both these assumptions may be in part true. In determining this question, or the greater probability of one or other assumption, the source of that prevalence of cholera which became manifest in the eastern Somali ports in April, and which is believed to have reached them from inland, becomes of great importance.

Neither the "North Wind" nor the "Persia" touched at any African port in the Gulf of Aden, or in the Red Sea between Makallah and Jidda. From the date of the "Persia" leaving Makallah (16th February) to the close of the north-east monsoon in March, communication by native craft could be maintained between that town and the east coast of Africa and the southern shore of the Gulf of Aden. Assuming cholera to have been present at Makallah, or in the vicinity, at the period in question, there were possibilities of its dissemination on both the eastern and northern coasts of the Somali country towards the end of February and the beginning of March.* Whether such chances of dissemination as are here indicated may have been concerned in the infection of the Somali country, will be best estimated after another, and, in this case, very probable, source of infection, now to be described, has been considered.

Epidemic cholera in Hindostan, 1863-1864.

Hitherto I have said nothing of a series of facts of which the different occurrences of cholera, that have been described in Arabia and East Africa, appear to me the continuation as well etiologically as chronologically.

In 1863 cholera became epidemic in the Lower Provinces, Bengal Presidency, and in the course of that and the two following years, it invaded the Central Provinces, the Bombay Presidency, the whole of Southern India, and Ceylon. The disease was epidemic in the Bombay Presidency in 1864–65, and in several districts it prevailed with unaccus-

* Dr. Christie doubts whether any dhow would venture to make any of the eastern Somali ports in February. He writes to me, of these ports, that "they are open roadsteads, and even in calm weather, tremendous seas roll in on the coast. A vessel becalmed near the coast, would be in the greatest possible danger. Dhows run regularly fer Zanzibar at the close of the north-east monsoon, but they do not usually call at intermediate ports."

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Cholera in the Bombay Presidency, 1864–5.

tomed violence. In the island of Bombay the mortality from cholera this year had only once been exceeded, (namely, in 1850, "the great cholera year,"*) since a registration of deaths had been established in the island in 1849. The mortality from the disease in the island in 1864 was 4,588, an excess of 2,581 above the average of the preceding 10 years. In 1850 the mortality had been 4,729.

The number of deaths from cholera registered in the island of Bombay in the months of November and December 1863 had been 176 and 319 respectively. In January 1864 the number increased to 622, this great augmentation being followed by a decrease in each of the two succeeding months, the mortality again rising to 680 in April, and reaching a maximum of 837 in May. After this month there was a steady decrease of the deaths from cholera until October, in which month only 88 were recorded. In November the mortality from the disease again increased; in December 431 deaths were recorded; and in January 1865, 363.

Coincidently with, or following in quick succession upon, the recurring activity of the disease here noted in Bombay, cholera commenced spreading actively in the Western Coast districts, notably in Malabar. "So "early as February and March (1864) cholera began to move southward "through Mysore, and from the southern districts of Bombay territory "into the Bellary District, which had escaped. But the most marked "manifestation of cholera occurred in the Western Coast Districts, par- "ticularly in Malabar, where 40,000 of the inhabitants died. Cholera "began to be active all through the cold dry months of the beginning of "the year, and attained its greatest activity in June and July."† The distribution of cholera in the Bombay Presidency during 1865 is pretty accurately known,‡ this being the first year in which a registration of

* *Deaths in Bombay during* 1864, p. v. The year of the registration returns dates from the 1st February.

† *A Record of the Progress of Cholera*, 1870, *and Resumé of the Records of former Epidemic Invasions of the Madras Presidency*. By Surgeon-Major W. R. Cornish, F.R.C.S., Sanitary Commissioner for Madras. Madras, 1871, p. 23. Consult also as to Cholera in India, during 1863–64, Mr. C. Macnamara's *Treatise on Asiatic Cholera* (1870).

‡ DEATHS from CHOLERA in the BOMBAY PRESIDENCY, 1865.*

Divisions.	Population.	Deaths from Cholera.	Months of Greatest Prevalence.
Tana - -	900,000	7,963	May and June.
Surat - -	792,638	9,463	Do.
Kaira - -	586,606	5,800	May, June, and July.
Khandesh - -	822,476	14,598	Registration began on June 1, when they were 6,137.
Ahmednuggur -	1,252,789	15,609	April, May, June.
Poona - -	679,429	9,114	Do.
Sholapur - -	634,867	3,493	April, May, June, July.
Satara - -	858,022	6,878	April, May, and June.
Kaladgi - -	563,123	3,055	April, May, June, and July.
Belgaum - -	707,537	1,247	May, June, and July.
Dharwar - -	782,465	1,191	June and July.
N. Canara - -	394,040	327	No special period of prevalence.
Ratnagiri - -	685,372	2,250	May, June, and July.
Scinde — Karachi -	340,000	300	Registration began in August, when deaths 101.
Scinde — Hyderabad	630,300	1,850	Do. in July, when deaths 1,313.
Scinde — Shikarpur	650,304	37	Do. deaths July 23 and Aug. 14.
Upper Scinde -	47,955	—	——
Thur and Parkur -	127,035	—	——

* Report of Sanitary Commission for Bombay, 1865.

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deaths among the civil population was attempted to be carried out in the greater number of the districts. The disease was generally epidemic throughout the central and southern divisions of the Presidency. Judging from the death registers it was active in the coast district of Tana at the beginning of the year, and in the adjacent coast district to the north, Surat, it became active in February. The following month, March, it began to spread in the districts of Ahmednuggur and Poona, contiguous to Tana, inland; also, in the district of Sholapur. The epidemic activity of the disease became manifest in the districts of Satara and Kaladji, in April; in the districts of Belgaum and Ratnagiri, in May; and in the district of Dharwar in June. In other districts registration was not commenced until the disease was in full activity or on the decline. This was the case in the Hyderabad and Karachi divisions of Scinde. From Karachi cholera is stated to have passed into Beluchistan and thence into southern Persia, extending along the coasts of Mekran, Mogistan, and Laristan, and the north shore of the Persian Gulf as high as Alsaloo (Bander es Salih), reaching that point in September.*

The appearance of cholera in an active form and its subsequent extension in Hadramaut, in Yemen, and in the Somali country, contemporaneously with wide prevalence and active extension of the disease in the Bombay Presidency, and following in succession upon a westward movement of cholera which, beginning in the Lower Provinces, Bengal, in 1863, had extended in an epidemic form to the Bombay Presidency in 1864, suggests that the phenomena form a continuous and connected series. That such was the case and that the relationship, in the first instance, between the outbreaks in Arabia and in East Africa and the prevalence of cholera in the Bombay Presidency, was of the same sort as between the subsequent outbreaks in Egypt and the Hejaz, and between Europe and Egypt, I have no doubt. North of the Straits of Bab-el-Mandeb the carriage of the disease in the ordinary

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* Mr. W. H. Colvill, then Civil Surgeon at the Bushire Residency, under instructions from the Political Resident in the Persian Gulf, Lieut.-Colonel (now Colonel Sir) Lewis Pelly, made, towards the close of 1865, an inquiry regarding the progress of cholera, during the year, in the countries bordering on the Persian Gulf. For the purpose of this inquiry, so far as it related to the Persian coast, he travelled by land from Bushire to Bassidore. In a despatch from Bassidore, dated 19th January 1866, he thus describes the results of this part of his inquiry: "Advancing "from India along the Meckran coast [cholera] was reported, in the end of last "May, to have reached Meenao, a highly cultivated district, with a village of about "2,000 inhabitants, situated on the Persian side of the Gulf, 60 miles eastward from "Bunder Abbas. In that month the heat at Bunder Abbas was intense, and on the "first report of cholera most of the inhabitants fled to Meenao. For that reason, "perhaps, the epidemic visited that town [Bunder Abbas] but slightly. From "Bunder Abbas, cholera proceeded inwards towards Shiraz, and onwards along the "Persian coast. Proceeding inland in the direction of Shiraz, it visited, but not "severely, the villages Jaharan, Fasa, and Darab, where it ceased. In no instance "has it appeared on the tableland of Persia. Proceeding onwards along the coast "and northern shore of the island of Kishm, it reached Lingah in August, and "remained there 75 days. Taking the average of numerous statements, it would "appear to have carried off about 10 per cent. of the inhabitants. For three conse- "cutive days 40 people it is said died daily. Immediately to the north-west of "Lingah is a district called Bunder Kunderoon, containing numerous villages, "lying round a salt marsh. In this district there are about 3,000 families, and 200 "people died of cholera. Charrack, with 300 families, did not lose more than "10 people, and from this the epidemic confined itself to the villages immediately "on the shore. At Cheroo it remained 45 days, and out of 400 people 40 died. "Nachilo, a village of 60 families, lost from 15 to 20 persons. The town of Nabend "escaped, but Assaloo, containing 400 people, lost two men and five women. And "here cholera ended on the Persian coast. In all these villages the nearest ap- "proach to time that can be given is that the epidemic appeared during the cutting "of the dates."

course of traffic or of pilgrimage was the observed initial fact of diffusion ; south of the Straits it is to be assumed that the same rule of dissemination held good. The epidemic which began in the Lower Provinces, Bengal, 1863, and spread very generally in the Bombay Presidency in 1864, has been described as extending during that year, especially in Western and South-Western Hindostan. Northwards it reached as high as Scinde ; southwards, overpassing the boundary of the Bombay Presidency, it passed as low as the extreme limit of the peninsula, in Travancore, and invaded Ceylon. This extension, on the north, as already stated, continued the subsequent year, and passing beyond Scinde extended to the coast of Mekran, and along the north side of the Gulf of Oman and of the Persian Gulf. The coast-line of the great tract of country thus infected overlaps, so to speak, the southern coast of Arabia, and the coasts of the Somali country ; and between the different coasts a considerable native traffic is maintained. This traffic, except on the Indian coast, and then only in a few large ports, escapes close observation, but its agency in the interchange of infectious diseases, as well as of materials of native commerce is well understood. It is highly probable that the coasting traffic played the most considerable part in the dissemination of cholera along the West Hindostan and Beluchistan and Persian coasts in 1864–65. Outbreaks at Cochin in February and September of the former year were in each case preceded by the arrival of ships with infected crews from northern ports. The two infected slave dhows captured by the " Penguin " when running north from the East African coast for the Arabian coast, illustrate the important part which this traffic may play in the interchange of infectious diseases on the coasts where it occurs. Facts of transmission from the Indian coast to the Arabian and Somali coasts, must necessarily, from the nature of the native traffic, and from our little knowledge of the ports to which it is directed be unattainable ; but it is known that the Arabian, the Persian, and the East African ports import into Bombay small-pox, and it is to be inferred that any infection current in Bombay may as certainly be exported to the ports of the several coasts named. Indeed, such exportation appears to extend to ports in the Red Sea as high as Jidda, for Mr. Stanley, who was Her Majesty's Consul there for five years, and Mr. Henry H. Calvert, who held the same post at the time of the appearance of the cholera in the Hejaz in 1865,* both have stated that cholera is imported into that town from India on the recurrence of every pilgrimage.

It is in the highest degree improbable that the movement of cholera westward from the Lower Provinces, Bengal, through Central India, into the Bombay Presidency would be arrested at the coast. The great dispersion along the coast line, north and south, implies a like extensive movement seawards, facilities existing for the propagation of the disease in that direction. Such facilities are mainly afforded by the native craft trading to Arabia and East Africa, but with them they occur only at one period of the year, namely, at the time of the north-eastern monsoon. These craft make one voyage out and home annually for the northern ports and Berbera, and leave the Indian coast, as a rule, with the earliest setting in of the monsoon. Few native craft would delay, till the close of the monsoon, sailing westwards to these places from Bombay, and other ports in the Bombay Presidency, which might have begun to suffer from the commencing epidemic of 1863. It is quite possible, however, that cholera may have been introduced into Berbera and carried inland at the termination of the fair

* Mr. Calvert was Acting Consul at Jidda from November 1st, 1864, to July 8th, 1865.

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of 1863–64. But the opening of the monsoon, in 1864, coincided with the reawakening activity of the disease and its wider prevalence on the coast and in the Presidency. In view of the active diffusiveness cholera was then manifesting, the transmission of the disease seawards by native craft at that time, and its importation into Arabia and East Africa, notably at Berbera, becomes almost as certain as if all the details of the process had been witnessed step by step. Indeed, there is not wanting some evidence of such importation into Arabia. Mr. Raby, when, in 1866, making inquiries for the International Sanitary Conference concerning the outbreak of cholera in the Hejaz in 1865, received information, the accuracy of which he was unable to determine, of the existence of the disease in Sana and other places in Yemen towards the close of 1864. Moreover, Dr. Dickson, the physician to Her Majesty's Embassy, Constantinople, submitted to the Conference information derived from letters from the Governor of Yemen in 1865 (Ahmed Pasha), addressed to his family, which he believed established the presence of cholera in that province before the epoch of the pilgrimage. This conclusion, Dr. Dickson informs me, was afterwards confirmed by testimony derived from native sources.*

Conclusions as to source of diffusion.

Reviewing the different facts and considerations which have been advanced, they appear to me to lead to the following conclusions :—

1. The infection of Mecca and the Hedjaz with cholera in 1865 was part of a wider infection, including Yemen and Hadramaut, in Southern Arabia, and the Somali country, in East Africa.

2. The infection of Yemen, Hadramaut, and the Somali country preceded the infection of the Hejaz.

3. This infection was a continuation of the epidemic movement of cholera westwards which, beginning in the Lower Provinces, Bengal, in 1863, had extended the same year through the Central Provinces into the Bombay Presidency, and spread along the whole western seaboard of Hindostan in 1864 and the beginning of 1865.

4. Although the details of transmission necessarily escape observation, it is to be inferred that the infection was carried seawards during the north-east monsoon, in the ordinary course of native traffic, and towards the close of 1864 (if not at an earlier period of the diffusion) was imported into Yemen, Hadramaut, and the northern Somali country.

5. This view, in accordance with the reported presence of cholera in Yemen near the end of 1864, and its probable presence in Hadramaut early next year, most satisfactorily explains, so far as the facts are known, the concurrent infection of both the Arabian and the African coasts of the Gulf of Aden.

6. The part played by the "North Wind" and the "Persia," whether these ships contracted the disease at Aleppy or at Makallah, was but a prominent early incident in the transmission of cholera from Hadramaut on the one hand, or from the west coast of India on the other, into the Hejaz.

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* I have the gratification of stating that Captain Richard F. Burton, who has lately proceeded on a mission to Sana, has most willingly and kindly undertaken to obtain such information as may now be practicable concerning the presence of cholera in that city, and in Yemen generally and Hadramaut, at the period under consideration. He will also endeavour to procure direct information respecting cholera at Berbera during the fair of 1864–65. This is the first opportunity of which I have been able to avail myself since 1865, of getting information respecting cholera in Yemen on the spot, Captain Burton has at all times taken an interest in inquiries of this kind, as is amply shown in his various works of travel; and his rare power of observation and command of languages may probably enable him to set definitively at rest the questions relating to the mode and time of introduction into Southern Arabia of the epidemic of cholera which forms the subject of this report.

7. The early manifestations of cholera in the ports of Yemen on the Red Sea in 1865, preceding the appearance of the disease in the Hejaz, probably arose in part from groups of infected pilgrims landing there, on their way to Mecca, from the Berbera fair.

8. Mecca and the Hejaz, indeed, were exposed to infection, and were most probably infected from the several sources following ; namely, (*a*) from the transmission by land routes from Yemen, and by sea from the ports of Hadramaut, of cholera imported into those provinces in 1864 or early in 1865; (*b*) from the northern Somali country by traders returning from the Berbera fair and the pilgrims accompanying them in March and at the beginning of April ; and (*c*) from Western India direct by way of Jidda.

9. So far as the infection of the Arabian coast is effected by native trading craft it almost wholly escapes observation, and even at Jidda it hardly admits of regulation. Any recommendation designed to limit the introduction of cholera into the Red Sea ports which fails to provide for the supervision of native trading craft must necessarily be fallacious.

10. The recommendation of the International Sanitary Conference of 1866, that a sanitary (quarantine) station should be established at the mouth of the Red Sea, was founded on the belief that the principal danger to the Hejaz from infection of cholera was the direct importation of the disease from India and the Eastern Archipelago, a belief not supported by the more complete knowledge which now exists of the conditions under which the infection of the Hejaz in 1865 took place. A sanitary (quarantine) station at the mouth of the Red Sea, would enable some sort of supervision to be maintained over pilgrim-carrying ships ; but there is no sufficient probability that the good it might effect would be at all commensurate with the difficulties attending its establishment, maintenance, and working. Indeed, as a sanitary station, it is little likely that such a system of medical inspection over the pilgrims and separation of the sick could be carried into operation as would be at all worthy of confidence, and as a quarantine station there is no good reason to believe that quarantine would be more efficacious here than it has been elsewhere where its restrictions being applied to one source of danger, other sources not less perilous have been left unfettered.

II.—The Outbreak at Mecca in 1865.

Pilgrimages in relation to the Diffusion of Cholera.

The outbreak of cholera at Mecca in 1865 was one of several outbreaks having certain characters in common, which had happened in the progress of the epidemic westward from India. At Mecca, indeed, existed on a gigantic scale, when cholera broke out there with greatest intensity, conditions especially favourable to the active maintenance and subsequent diffusion of the disease, but which, with one exception, were not peculiar either to the locality or to the pilgrimage. If the particular foulness of the period of sacrifices be excepted, there were no states of filthiness, over-crowding, fatigue, or ill-feeding which could not then be paralleled by like states during the great Hindoo pilgrimages, and of which the filthiness and overcrowding, at least, were not also common to those great Eastern fairs which are not religious festivals. Competent observers have advanced reasons for the belief that cholera would rarely occur in a pestilential form in many districts of India, and perhaps die out in some, if it were not that the disease, when it becomes epidemically diffusive, is in effect cultivated by the annually recurring religious festivals.

The earliest information I have met with relating to the epidemic extension of cholera in 1863–64 in the Bombay Presidency refers to

the religious festivals or fairs of Punderpoor and Alandi. Two fairs are held yearly in each of these places, one in July and one in November. Punderpoor is a town, in the Satara collectorate, situated on the river Bheema, 31 miles from the Barsi Road station of the Great India Peninsula Railway, which has become "the main feeder of the pilgrimage."* It had in 1851 a permanent population of 14,000, living in 2,100 houses. Alandi is a small village, in the Poona collectorate, situated on the River Indrayani, 13 miles north of Poona. It has a permanent population under 2,000 in number, living in 200 houses. The pilgrims who resort to each of the annual fairs at Punderpoor are estimated to average in number 50,000; at Alandi upwards of 20,000. At certain of the Punderpoor fairs the number of pilgrims has exceeded 100,000, and is believed to have been not less than 125,000. Notwithstanding the long-continued efforts of the Bombay Government, dating from a period before that now under consideration, to ameliorate the condition of the pilgrims congregated at the fairs as to filth and over-crowding, and generally to subject the rites and the unwholesome states incident to them to sanitary regulation, the fairs are still a constant source of anxiety from their liability to become centres for the development and diffusion of infectious diseases. Many of the pilgrims who visit Punderpoor commonly visit Alandi also, so that the one fair at times is apt to intensify epidemic mischief started in the other. This appears to have been the case in November and December 1863, when, according to one observer, although cholera had shown itself in an aggravated form at Punderpoor, it was at Alandi, after the arrival there of pilgrims from Punderpoor, that the disease first showed that epidemic diffusiveness which in the two following years characterised its course in the Presidency.† Dr. Haines, the superintendent of mortuary returns for Bombay, in his report for 1863, after indicating the Deccan as the probable source of previous infections of Bombay with cholera, observes: "But that the great outbreak in December last [1863] "was due to contagion imported thence there can be no reasonable "doubt. For days before the disease broke out here it was notorious "that the pilgrims returning from the fairs of Punderpoor and Alundee "[Alandi] were dying by hundreds, and the introduction by them of "the disease into the city of Poona was greatly dreaded, and not "without reason. It soon appeared there, carrying off scores daily, and "very shortly afterwards the rapid increase of cholera in that town "showed how quickly the contagion spread along the ordinary line of "traffic."‡

The re-commencing activity of the epidemic in the Bombay Presidency in 1864 appears to have been first especially noted in the

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* See on Punderpoor (Pandharpur) and Alandi, and the religious festivals there, *The 10th Annual Report of the Sanitary Commissioner for the Government of Bombay* (1873), *Section V.*

† The Rev. Adam White, who visited the festival at Punderpoor in November 1863, and who lost his life from cholera at a subsequent period of the epidemic, wrote in January 1864 as follows:—

"The day after I left Punderpoor, cholera in a bad form manifested itself among the pilgrims, but many did not die. The disease might have died out if it had not been cultivated. But the same pilgrims immediately resorted, as is their wont, to Alandi near Poona, and there it met with a favourite field in which to grow. The seed sown at Punderpoor ripened quickly and fearfully at Alandi, and the grain was thus scattered broadcast over the length and breadth of the land by pilgrims on their way home. Poona was one of the first places to suffer, and a vast number died in it. The moment the returning pilgrims reached any field of labour [sassoor], the disease appeared and people began to die. . . . . Every village almost had its tales to tell."—*Deaths in Bombay*, 1863, p. xiv.

‡ *Deaths in Bombay*, 1863, p. xi.

Khandesh collectorate at Mahiji (Mhyjee). This small town, situated on the Great Indian Peninsula Railway, about 30 miles east of Dhoolia, is the seat of the largest of the fairs in the Presidency, devoted entirely to internal trade. Here, in February, after the commencement of the fair, cholera broke out violently, and the disease is described as having "raged severely," while the fair continued, during that and the subsequent month. Again, in 1865, an important part has been assigned to pilgrimages in determining early epidemic activity of cholera in that year.* In these instances, as in the outbreaks on board the pilgrim-carrying ships off the coast of Hadramaut, the epidemic manifestation of the disease may be said to have been precipitated, as it were, by the conditions under which the outbreaks occurred.

It would have been instructive, had it been possible, to have followed in some detail the history of the westward propagation of cholera during 1863–65, to the time of the outbreak at Mecca, in relation to religious and commercial fairs. But at this period there was no connected account of the movements of cholera among the civil population of the three Presidencies of Hindostan, and only such scattered information on the subject as that of which I have given a sample appears to be obtainable. This, however, is sufficient to indicate that events of development and diffusion, such as I am about to describe of the outbreak of cholera at Mecca, are common to all these gatherings at periods when cholera becomes diffusive, as are the conditions which determine them. Our knowledge is still very inadequate of the influence which the great religious gatherings at Nedjef (Meshed Ali), at Kerbella (Meshed Hussein), at Meshed and other centres of pilgrimage in Irak Arabi and Persia, may have exercised in favouring the transmission of cholera to Europe in the different invasions to which the Continent has been subjected. Meshed lies on the great northern trade route from India to Persia and the south shore of the Caspian; Nedjef and Kerbella on the route by way of the Persian Gulf and Irak Arabi. There are some grounds for the belief that the pilgrimages to these places may have exercised a hardly less important influence upon the propagation of cholera to Europe in previous invasions than was exercised by the pilgrimage to Mecca in 1865. I shall have to show presently these widely separated places re-acting on each other in the propagation of cholera, and forming during times of pilgrimage centres in which the disease may take on fresh activity.

Outbreak at Mecca in 1865.

At what date cholera first appeared in Mecca, in 1865, is not known.† Rumours of an unusual mortality among the pilgrims had reached Egypt

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* The following, with reference to 1865, is from Dr. Bryden's work, *Cholera Epidemics of Recent Years* (1874, p. 121):—"Colonel Keatinge writes to me from "Kattywar in June 1865: 'There is much cholera in the south-east of the pro-"vince. There was a fearful outbreak at the close of a great concourse of pilgrims "'at the Palectana Hill in the cold weather, and it has lingered ever since. Our "'invalids and time-expired men from the Punjab who went down the Indus met "'this cholera as soon as they arrived at Kurrachee in the early months of 1865.' "..... In the introduction to the 'Deaths of Madras,' for 1864, it is "'mentioned that in these months of 1865 the high road leading from Nagpore "'to the terminus of the Bombay railway had been literally a valley of death." The following extract is from this report: "During the past year (1864) and the "present (1865), two fearful epidemics have taken their origin from the same "spot (the Temple of Mahadeo)."

† Mr. C. Macnamara writes as follows upon this subject:—"My friend, Saeed "Bukht, of Sylhet, who has lately been in Calcutta, but who was a member of the "local council of Mecca in 1865, assures me that cholera did not exist in or about "the city before the end of March 1865. On the 24th and 25th of that month he

THE OUTBREAK AT MECCA, 1865.

in March, and in April the Egyptian Board of Health sent a medical commission, consisting of two Mahommedan physicians, to the Hejaz, to ascertain the actual state of things there. This commission reached Mecca just before the commencement of the rites of pilgrimage, and, according to a report dated the 10th May 1865, they found cholera prevalent among the inhabitants of the city, the soldiery, and the pilgrims. Many dead were seen lying in the mosques, and some in the streets. The disease was most prevalent and fatal among the pilgrims the third day of the rites, during the assemblage on Mount Arafat, the 2nd May. The deaths in Mecca the same day were estimated at 200. An Ottoman sanitary commission, sent to the Hejaz to investigate the outbreak, reported several months afterwards that the disease "broke out" in the valley of Muna during the second day of the sacrifices (4th May), referring probably to the period of assumed greatest prevalence of the disease. According to this commission the number of pilgrims assembled at Mecca was 100,000, and the mortality from cholera among them was from 10,000 to 15,000. The International Sanitary Conference of 1866, from the information in its possession, came to the conclusion that more probably the mortality was double that amount, the number of pilgrims, according to Mr. Henry H. Calvert, not exceeeding 90,000.

There is no reason to believe that the conditions under which the rites of pilgrimage were performed in Mecca in 1865, differed in any material degree from the conditions described by Burton in 1853*, and by Burckhardt† at an earlier date. It was not until after the outbreak of cholera there in 1865, and as one of the consequences which followed from it, that the Ottoman Government instituted systematic measures for the sanitary regulation of the pilgrims during the performance of the rites. In 1865, it is to be inferred that, as in previous pilgrimages, there were congregated at Mecca, while the different observances of the pilgrimage were being accomplished, a large proportion of the way-worn, the exhausted, and the starving; and that from the greater number of pilgrims assembled that year the over-crowding of the city and the encampments would be greater, as also, if this were possible, their indescribable foulness, a foulness from the stench of which even the

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" states that rain fell over Mecca, and about the same time cholera broke out among " the assembled pilgrims. Few men are better acquainted with the phenomena of " the disease than Saeed Bukht; being a native of Lower Bengal he had seen cases " of it year after year from his infancy, and is, moreover, a remarkably shrewd and " keen observer. He is well aware of the history of the ships 'Persia' and 'North " Wind,' in connexion with the outbreak of the disease at Mecca, and his remark " on the subject to me was, that very likely cholera was introduced by the infected " pilgrims arriving in these vessels. But who can say when there were so many " thousands of men coming and going?" The completion of the paragraph from which the above is quoted is of much interest, showing that Mr. Macnamara, working independently in India at the question of origin of the diffusion of cholera, considered in this report, arrived substantially at the same conclusion as myself working in this country. He continues: "Moreover I have already shown that the disease had " spread from Bengal into Central India and Bombay in 1864, and had been " reproduced over the whole of that territory with extreme virulence in 1865; and " further, that early in the year it was known to be prevalent along the sea coasts " of Arabia and the western shores of the Red Sea, having, doubtless, extended " from the various ports in the Bombay Presidency, as it had done on every pre- " vious occasion when it visited Arabia and the shores of the Red Sea, notably " as described by Ruttonjee Hormusjee in 1858."—*A Treatise on Asiatic Cholera*, by C. Macnamara, 1870, pp. 203–4.

* *Personal Narrative of a Pilgrimage to El Medinah and Mecca*, by R. F. Burton, 3 vols., 1855–6.

† *Travels in Arabia*, by J. Lewis Burckhardt, 2 vols., 1829.

almost stench-proof Arab of Mecca seeks protection by plugging his nostrils with cotton.

No detailed account has been published by any eye-witness of the events which happened at Mecca and in the several localities where the rites are performed during the days devoted to them. It is simply known that the great mortality from cholera happened in the course of the six days over which the rites extend, while the pilgrims were at Arafat, and in the valley of Muna. Probably two-thirds of the whole number of deaths took place in this brief space of time. The streets of Mecca, its mosques, the twelve miles of road lying between the city and Mount Arafat, the valley of Muna, and the plain of Arafat were cumbered with the dead. At all times the exhausted pilgrim is apt easily to yield up life. To a fatal infection like cholera he succumbs unresistingly. Death on the sacred soil is to him but the passage to beatitude.

The last day of the rites in 1865 was on the 6th May, and the pilgrims, panic-stricken by the ghastly mortality, hastened to leave Mecca. When my first report was written, the events which had occurred on the homeward route of the pilgrims who journeyed to Egypt by way of Jidda and the Red Sea, and onwards from Egypt by way of the Mediterranean, were alone known and these not fully. The events which occurred among the bodies of pilgrims travelling homewards on the northern and eastern pilgrim land-routes, have since been ascertained to some extent; but of the events occurring among the pilgrims travelling by the southern pilgrim routes nothing is known. On all the routes of which we have knowledge of what happened on the passage of the returning pilgrims cholera was carried in their train. It was thus carried along the northern sea-route to Egypt and Nubia; along the northern land-routes into the desert to some of the desert towns; and along the eastern land-route through Central into Western Arabia. I proceed to describe the order of appearance of the disease on the several routes, and the succession of events which followed thereupon.

1. *The Diffusion along the Northern and Western Pilgrim Sea-Routes.*

The Diffusion to Lower Egypt.

The rites ended, in 1865, on the 6th May, and four days afterwards pilgrims returning from Mecca began to enter Jidda. There had been considerable mortality among them from cholera on the journey. The pilgrims bound seawards hastened to embark for their several destinations, and on the 19th May the first ship bringing pilgrims from Jidda arrived at Suez. About the same time, it is to be inferred from subsequent events, vessels with returning pilgrims bound for Kosseir and Suakin arrived in those ports.

The appearance in Suez, May 1865.

The ship which reached Suez from Jidda on the 19th May, was an English steam vessel, crowded with 1,500 pilgrims. At this time no suspicion existed in Egypt of any peculiar tendency among the population to diarrhœal disease, or of the existence of any choleraic malady other than might be of ordinary occurrence in the country at all times. Several days before the arrival of the ship in question, and before definite information had been received of the existence of cholera in Mecca, the Sanitary Administration had determined to adopt certain precautionary measures* with a view of preventing the introduction of

* Meeting of the 3rd May 1865.

disease into the country, by the returning pilgrims. Arrangements were made for a medical inspection of the different bodies of pilgrims as they arrived, for subjecting such of these bodies as might be found infected to quarantine, and for limiting to the shortest period the sojourn in Lower Egypt of pilgrims who were traversing the country to other destinations, preventing at the same time as far as practicable their intercourse with the population. To effect the latter objects, provision was made for sending these pilgrims on their arrival at Suez by express trains to Alexandria, and for embarking them there at once upon steam boats for their further destination. The first ship which orrived at Suez with pilgrims, as each of the subsequent ships, was inspected medically, but not a single instance of cholera or of sickness was observed on board, and no ship was in consequence detained in quarantine. So rapidly did these vessels succeed each other, that before the close of May from 12,000 to 15,000 pilgrims had been landed at Suez, and a considerable proportion of these had, immediately after landing, been sent by rail to Alexandria. The total number of pilgrims landed at Suez, returning from Mecca, was 18,490*. Among this great number of pilgrims the medical inspectors of the Sanitary Board failed to detect any signs of choleraic disease before they left ship-board ; and of the pilgrims who afterwards encamped outside Alexandria waiting embarkation for other ports, indications of much fatigue were alone noted. It is not easy to conceive what sort of medical inspection is possible of masses of such men as these pilgrims are, made on the crowded deck of a ship or in a hardly less crowded encampment, under the condition that the delay necessary for proper observation shall only be interposed if the disease for which the observation is made shall be there and then found. It is obvious that an inspection of this kind can only apply to very marked appearances of disease, and that it is altogether illusive, as proved to be the case here, as regards appearances less manifest, but not less dangerous to the safety of a community.

After the pilgrims landed at Suez those who dwelt in Lower Egypt proceeded at once to their several destinations, many travelling by rail, and, as customary, the people of the places through which they passed, and at the railway stations where they alighted, crowded to salute the happy men fresh from the sacred soil of Mecca. Whatever precautions may have been taken to limit, during the journey, intercourse with such of the pilgrims as were hurried by express trains to Alexandria in order to be embarked for other parts, no restriction appears to have been placed upon communications between them and the inhabitants of the city, while they remained encamped in the vicinity.

Events quickly proved that cholera had not so completely died out among the pilgrims after leaving the Hejaz ports as had been assumed from the cursory inspections at Suez and Alexandria. It is highly probable that the disease was so nearly upon the point of extinction, that a few days longer voyage in the Red Sea, or a brief period of detention under observation, might have brought about its cessation, had not the infection been introduced among a population of which the susceptibility to cholera was fresh. But that the infection existed among the pilgrims, and was introduced in their train into Egypt, is proved by the following facts.

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* From Jidda - - - 10,125
From Yembo - - - 8,339
From Suakin - - - 26

18,490

THE DIFFUSION FROM MECCA NORTHWARDS & WESTWARDS, 1865.

The first ship carrying pilgrims returning from Mecca arrived at Suez, as already stated, on the 19th May 1865. During the voyage there had been six deaths among the pilgrims, from unascertained causes, and the bodies had been thrown overboard. On the 21st May, the second day after the ship's arrival, the captain and his wife were both attacked with cholera. The cases were observed by Dr. Papathodor, a medical man in the service of the Isthmus of Suez Canal Company, but neither case appears to have been fatal. On the 22nd May, Dr. Fibich, another medical man in the service of the same company, saw a case of cholera at Damanhur, 46 miles E.S.E. of Alexandria, and on the line of railway from Suez, among a body of pilgrims coming from the last-mentioned port.

The appearance in Alexandria, June 1865,

On the 2nd June a case of cholera (the first recognised) occurred among the inhabitants of Alexandria who were in communication with the pilgrims. On the 5th June two other cases occurred under the same circumstances. From this date cases became more numerous, but until the 12th June, according to Dr. Aubert Roche, Principal Medical Officer of the Suez Canal Company, they were confined to that portion of the population which was brought into contact with the pilgrims.*

On the 11th June the presence of cholera in Egypt first became known to the Sanitary Administration, and the next day (the 12th) four deaths from the disease were officially reported in Alexandria. The patients among whom these deaths occurred were porters and labourers attached to the railway, who, from the nature of their duties, and the position of their homes, were necessarily in close communication with the pilgrims. The same day foul bills of health began to be issued to ships leaving the port. On the 13th June, 12 deaths from cholera were reported ; and on the 14th, 39.

and in Cairo,

On the 16th June, six cases of cholera were reported at Cairo, five of the patients being persons (it is not stated whether they were pilgrims) coming from Suez, who were taken ill at the railway station; the sixth was an individual living in the Lesbekieh quarter.

and Kosseir,

The same day a ship from Jidda arrived at Kosseir, carrying 73 pilgrims, four of whom were ill of diarrhœa, and two deaths (cause not ascertained) were reported at sea. No information is given of previous arrivals of ships from the Hejaz in this port, and official records simply mention that cholera began here " early in June."

and Suakin.

About this time it is to be inferred that cholera was present in Suakin, as on the 24th June the Egyptian frigate " Ibrahimée " arrived at Suez from that port with 12 of her crew sick of cholera.

Kosseir and Suakin were probably infected about the same time as Lower Egypt.

The subsequent diffusion of cholera in Egypt and Nubia, and the further spread of the disease in East Africa will be treated in another section.

There is no clear evidence of the carriage of infection by the pilgrims embarking at Alexandria to other points in the basin of the Mediterranean. Where, on the one hand, the lines of transmission coincided with the passage of pilgrims, as at Malta, Marseille, and Beyrout, they

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* The authority for these statements is Dr. Aubert Roche, the Principal Medical Officer of the Isthmus of Suez Canal Company at the time. See his *Rapport sur le Choléra dans l'Isthme de Suez en Juin et Juillet* 1865, p. 12.

coincided also with the passage of numerous persons, many of them fugitives, from the freshly infected population of Alexandria. Moreover, in no instance along those lines of transmission is it reported that the first imported or occurring case was a pilgrim. On the other hand, no infection, as far as is known, followed in the train of the pilgrims who landed in Tripoli, Algeria, and Morocco; but there were several instances of infection accompanying ordinary passengers from Alexandria to ports along the lines of traffic not followed by pilgrims, as to Ancona, Valencia, and to Southampton. It is impossible to say that the pilgrims had no part in the diffusion of cholera from Alexandria on the shores of the Mediterranean, but the evidence indicates that the diffusion was mainly, if not wholly, effected by persons originally coming from the new centre of dissemination set up at Alexandria. The direct agency of the pilgrims in carrying onwards the disease ceasing after they had embarked at Alexandria, or being inseparable from the concurrent agency of fresh carriers coming from the new centre of infection there, the further history of the diffusion on the shores of the Mediterranean will be treated in another section.

2. *The Diffusion along the Northern Pilgrim Land-Routes.*

The diffusion to Medina, and Northern Arabia.

The facts ascertained respecting the diffusion of cholera from Mecca along the northern pilgrim land-routes are very few and incomplete. At this time attention was so much absorbed in the spread of the disease in Egypt and Syria, and in its extension to Europe, that little heed was given to the facts of its prevalence or absence in the caravans travelling by land northwards. Moreover, the pilgrimage was not subjected in 1865 to such close sanitary observation in the Hejaz as it is now subjected to, and which has admitted since that year of a fairly detailed knowledge of the sickness and mortality among the pilgrims in their progress from Mecca to their different destinations while within the Ottoman and Egyptian dominions.

Dr. Martini, a physician in the service of the Egyptian Sanitary Administration, visited Yembo in the second week of June (1865). He found there 5,000 pilgrims waiting embarkation without any prevalent sickness among them, and received information from, he believed, trustworthy sources that cholera had ceased among the pilgrims after they had left Mecca.

The Damascus caravan entered that city on its return journey on the 17th July, having started from Mecca on the 6th or 7th June. The caravan had been medically examined at Mejarib before entering the city, and it was certified that no case of cholera had occurred among the pilgrims since they had left Mecca.

Seven caravans on their way to Lower Egypt, by way of Suez, were examined at El Wedj. The first, consisting of 850 pilgrims and 2,800 camels, entered El Wedj on the 11th June, no ailment existing among the pilgrims, except two cases of diarrhœa. The second caravan, consisting of 1,000 pilgrims and 1,500 camels, entered El Wedj on the 8th July, and excepting three cases of diarrhœa the pilgrims were healthy. The three other caravans, containing together 2,950 pilgrims and 4,500 camels, all entered El Wedj on the 9th July with but three sick of diarrhœa among them.

On the 4th July 1865 the Sanitary Office at Bagdad received information that vomiting and diarrhœa had been observed among the pilgrims returning from Mecca by way of Medina and the desert route

to Nedjef (Meshed Ali). This route divides, after leaving Medina, into two branches, which unite again at Haiel, in Jebel Shomer. The western branch proceeds by way of Khaibar, the eastern by way of Aneyzeh, Bereydeh, and Kaseem. At Bereydeh this last-named branch joins the route leading from Haiel to Riad, and here pilgrims returning from Medina into Central Arabia, and travelling through Nejed and Hasa homewards, diverge from the northern desert route for Nedjef. Cholera, following upon the passage of pilgrims from Mecca, is reported to have appeared in succession at Medina and Aneyzeh, and to have passed from the latter town to Riad. Here the disease entered the eastern pilgrims' land-route, of which, indeed, the route from Riad to Aneyzeh is a branch. Nothing is known of any prevalence of the disease in Jebel Shomer, but the pilgrims who travelled to Nedjef along this route, as the pilgrims who travelled by the land routes to Yembo, El Wedj, and Damascus arrived at their destination free from the disease.

3. *The Diffusion along the Eastern Pilgrim Land-Route.*

The diffusion to Central and Eastern Arabia.

The history of the diffusion along this route, although it can be described only in general terms, is of peculiar interest. In 1865 Lieut.-Colonel (now Colonel Sir) Lewis Pelly, then Her Majesty's Political Resident in the Persian Gulf, visited Riad, the capital of Nejed, Central Arabia. He was accompanied, among others, by Mr. Colvill, then attached as civil surgeon to the Bushire Residency, and left Koweit (Grane) for the interior on the 18th February, returning to the Gulf by way of Okair on the 18th March. At this time although cholera was extending along the coast of Mekran, and was probably present in Southern Arabia, and certainly present in the northern Somali country, not a whisper of the disease was heard in Riad. On the return to the coast the expedition sighted a party of pilgrims for Mecca, who had landed at Kateif, and were on their way to Riad. Colonel Pelly estimated the number of pilgrims passing annually through Nejed to Mecca as 32,000, of whom 2,000 entered the country by way of Koweit, the remainder by way of the ports of Hasa. At the time when cholera appeared in Nejed, Eastern Arabia, north of Oman, was free from disease. There is no information regarding the pilgrims who travelled homewards on the direct route from Mecca to Riad, but it is to be inferred from the events which happened on the other pilgrim-routes that they would not be wholly inactive in propagating the disease. The outbreak of cholera in Riad was severe, and from that town the disease was propagated in a north-east direction to the head of the Persian Gulf. Mr. Colvill, in the despatch to which I have already referred (see foot-note, p. 22) describes the progress of cholera from Riad as follows :—"Cholera now passed north-north-"east through the various tribes under the Wahabee rule, to a small "place called Jaharah. This is simply a large farm belonging to a "merchant of Koweit. It is 20 miles west of that town and 70 miles "from Busreh (Basra). It consists of three enclosures close together, "containing about 200 inhabitants; but at this time the Mutyr and "Beni-Khalid tribes, tributaries of the Wahabees, were encamped round "it to the number of 4,000 or 5,000 tents, with the intention of "attacking a portion of a Bedouin tribe called the Dthefye, which was "encamped at Isphuan, a watering-place 30 miles on the road to "Busreh. Cholera visited the Mutyr and Beni-Khalid tribes severely. ". . . The epidemic next appeared, on the 25th and 26th of August, "at Duaseh. This is a village situated on the right bank of the Shat-

THE DIFFUSION FROM MECCA SOUTHWARDS & EASTWARDS, 1865.

"el-Arab, about 40 miles below Busreh."* Cholera was first recorded in Basra on the 27th August; and its presence in Koweit and Mohammera was reported early in September.

Meanwhile the pilgrims in various groups were making their way to Nedjef and Kerbella along the northern route through the desert, and along the route through Nejed, some on the latter route by way of Koweit, others by way of the Hasa ports. The pilgrims began to arrive in Nedjef about the middle of July, and the last caravan entered that town towards the close of August or at the beginning of September. All the caravans were reported free from choleraic disease on their arrival at Nedjef, except the last, among which two cases were observed. This caravan had passed up the Euphrates at a time when cholera was present on both banks of the river, preceding caravans which had followed this course, before the appearance of the disease in the vicinity of Basra, having, it is reported, had no cases. The great caravan, as the Damascus caravan, was reported free from sickness during the whole of its journey, but it was ascertained that several deaths had happened on the way, although neither the cause of the deaths, nor the period of the journey at which they occurred, was discovered. After leaving Nedjef and Kerbella, the pilgrims who took the road by way of Hillah and Bagdad to Persia showed no signs of infection in the different towns through which they passed, and those who stayed in Bagdad remained free from the disease.†

On the eastern pilgrim land-route, as on the northern sea route, the propagation of cholera was mainly effected from the secondary centres of the disease set up by the pilgrims in the earlier part of their journey. The disease, so to speak, lagged behind the different groups of pilgrims as they advanced on their journey, and those who travelled by Jebel Shomer, were apparently disembarrassed of it before they had passed the desert, and those who had passed through Nejed before they had reached the Euphrates.

4. *The Diffusion along the Southern and Eastern Pilgrim Sea-Route.*

The International Sanitary Conference was of opinion that cholera had been carried to the Euphrates, and scattered on the southern and eastern coasts of Arabia by the pilgrims who returned homewards by the southern and eastern sea-route. At the time when the pilgrimage ended, and the return of the pilgrims commenced, cholera, as I have already shown, had been prevalent in Hadramaut, and was still prevailing on the east coast of Africa and in the interior of the Somali country, and on the coast of Mekran and the neighbouring Persian coast. Information received at Aden during the presence of the disease in the Hejaz indicated wide prevalence and great mortality in Hadramaut; and during July it was known at Bagdad that the malady was very fatal at Mascat, and probably in other parts of Oman. While cholera was thus

* See also on this subject, Mr. Colvill's "Sanitary Report on Turkish Arabia," published in the *Transactions of the Medical and Physical Society of Bombay*, 1871, p. 60. At the time when Mr. Colvill wrote his despatch of the 19th January 1866, he was unaware of the presence of cholera on the coast of Oman at the same time that it was prevalent on the opposite Persian coast, also of the occurrence of the disease at Koweit, and of the precise date of its first recognition at Basra. The statements in the despatch with regard to the two latter places requiring to be modified, I have not quoted them.

† Mr. Colvill, in the despatch previously referred to, states that cholera on the route to Nedjef and Kerbella was most severe among the pilgrims. The statements in the text are made on the authority of the reports furnished, at frequent intervals, from the different localities, to the Ottoman Sanitary Office at Bagdad, at the period to which they refer.

active in Southern Arabia, it was also extending along the northern coast of the Gulf of Oman and the Persian Gulf, Bunder Abbas suffering at the same time as Mascat. What part, if any, pilgrims returning by the sea-route to the coasts of Hadramaut and the Persian Gulf may have played in adding to the prevalence of previously existing cholera there, by importations of the disease from the Hejaz, it is impossible to say. Equally impossible is it to state what part importations from Oman and from the opposite Persian shore may have played in the development of cholera on the banks of the Shat-el-Arab, and of the Euphrates.

After the appearance of cholera at Basra in August, the disease passed along the Shat-el-Arab and the Euphrates, attacking the different towns in succession as it ascended the stream. At the same time cholera was descending the valleys of the Euphrates and Tigris, having entered them from northern Syria, high above the confluence of the two streams. The progress of the disease in the valleys of the two rivers, and its subsequent extension into Persia, will form the subject of a separate section.

III.—The further Diffusion.

I have now to take up the story of the diffusion at that point where the influence of the pilgrims returning homewards from Mecca as carriers of the epidemic had ceased, or was no longer to be distinguished from that exercised by persons coming from the new centres of diffusion set up by them. In dealing with this part of my subject I propose to describe the several principal developments of the diffusion in the following order, as, perhaps, best admitting of a connected view of its progress :—

1. The Diffusion to Europe and prevalence there from 1865 to 1869.
2. The Diffusion to the South and East Coasts of the Black Sea.
3. The Diffusion to the West Indies and North America.
4. The Diffusion to North-western Africa and to West Africa.
5. The Diffusion in Egypt, Nubia, and East Africa.
6. The Diffusion in Syria and Western Anatolia.
7. The Diffusion in Mesopotamia, Kurdistan, and Persia, and incidentally
   (*a*) The Diffusion in Arabia and Nubia in 1871–72 ; and
   (*b*) The Diffusion in Central Asia, 1871–72.

The recurrence of cholera in Europe in 1869, and its prevalence on the Continent during the four succeeding years, will form the subject of a separate section.

I.—The Diffusion to Europe and prevalence there from 1865 *to* 1869.

The Diffusion to Europe. I. The antecedents. Europe taken by surprise.

The Antecedents.—Europe was taken by surprise when cholera appeared in 1865 on the south coast of the Mediterranean, at Alexandria, and began thence to extend rapidly to the southern and eastern shores of that sea. It was not, indeed, until the disease had effected a lodgement in several parts of the Continent that the attention of governments and the public was fully aroused. In no previous epidemic had Europe been attacked from the south, and any danger from this source was looked for along the routes which cholera had travelled in the earlier invasions of the Continent. There had been no information of epidemic prevalence of cholera in Western India in 1864 and the beginning of 1865, following upon a movement of the disease through the Central Provinces, from the Lower Provinces, Bengal. Nor would such information have availed much had it been accessible ; for in the

THE ANTECEDENTS OF THE DIFFUSION, 1865.

event of the disease being propagated beyond the shores of Western India, its propagation would have been expected to follow the route which was traversed by the first great epidemic which invaded Europe in 1830, namely, along the Persian Gulf, and through Persia to the Caspian Sea and Russian frontier. But it was not until after the close of 1865, when cholera had already spread widely in Europe and crossed the Atlantic, that the real significance of the movements of cholera in Western and Central India in the years 1863–64 could have been fully understood. As already stated in a previous part of this report, 1865 was the first year of attempted registration of deaths among the civil population of the Bombay Presidency, and I may add, also, of parts of the Bengal Presidency. The following year (1866) a beginning of registration of deaths was made in the Madras Presidency. From and after this year only dates the possibility of viewing comprehensively the movements of cholera in India; but it may be still questioned whether it is even yet practicable to forecast the probable future of these movements in reference to other countries.*

No indications of coming pestilence admitting of forecast.

Not only from the experience of previous epidemics but, also, from the then necessary want of acquaintance with what was happening in India, was Europe unprepared for the invasion of cholera from the south, but there was nothing in the general state of health of the populations of the Continent to lead to the supposition that pestilence was impending. No augmentation of diarrhœal disease or marked deterioration of public health such as was believed to have preceded the epidemics of cholera of 1832–33, and of 1848–49, marked the appearance of cholera in 1865. It is true that in Egypt and in Southern Arabia the outbreak of cholera coincided with a period of much privation, arising from murrain among flocks and defective harvest from drought, but like privation was not present elsewhere among the communities attacked. It is true, also, that murrain had preceded cholera in Syria and in Europe, but its association with that epidemic was incidental not common and general. It is true, moreover, that in several places the coming of the epidemic is believed to have been foreshadowed by unusual prevalence of zymotic maladies and especially of gastro-intestinal affections. Thus, in Malta and Gozo, Dr. Sutherland has shown that of the class of maladies last named, there came under treatment in the public medical institutions of the islands no less than 6,263 cases during the first six months of 1865, as compared with 4,166 cases during the corresponding period of 1864.† He describes also an increase in the prevalence of fevers during the first six months of 1865. "These facts," he observes, "are sufficient to show that long before

The antecedents in Malta,

* See on this subject, and especially with reference to India, Dr. Bryden's elaborate report on "*Cholera Epidemics of Recent Years viewed in relation to former Epidemics: A Record of Cholera in the Bengal Presidency from* 1817 *to* 1872." *Calcutta,* 1874.

† RETURN of the NUMBER of CASES of certain kinds of SICKNESS observed in the Public Institutions of Malta and Gozo during the first six months of 1864, and the corresponding period of 1865 :—

	1864.	1865.
Dyspepsia and gastricism	1,915	2,086
Colic	595	777
Diarrhœa	1,042	1,243
Dysentery	465	559
Sickness and vomiting	149	180
Enteritis or gastro-enteritis	1,308	1,418
All other diseases	18,383	20,547

—*Report on the Sanitary Condition of Malta and Gozo with reference to the Epidemic Cholera in the year,* 1865, p. 12.

" cholera began its course towards the north-west there were indications " of a changed condition of the public health in Malta " (p. 14) ; and after giving an account of two groups of choleraic cases which occurred in May, he adds : " It appears to me scarcely possible to escape " from the conclusion that long before cholera appeared in Malta, " possibly before its first outbreak in Arabia, the earliest wave of the " coming epidemic had passed over these islands " (p. 15). But while, according to Dr. Sutherland, the coming epidemic was thus clearly foreshadowed in Malta, no change in the public health presaged its appearance in Gibraltar. In his report on the disease there in 1865, he *in Gibraltar.* shows that the number of cases of gastro-intestinal affections recorded in public medical practice among the civil population during the first six months in 1865 was less than during the corresponding period of 1864 (namely, 1,097 as compared with 1,129).* There was " no great " amount of diarrhœa among the troops ; " no febrile affections are referred to ; and, except three cases of violent diarrhœa among children in the town, no special events of sickness to note. He draws attention to " a slight increase of visceral affection " (referring apparently to the columns headed " sickness and vomiting " in the subjoined Table) in the earlier months of 1865, chiefly in May, June, and July of this year ; " but," he adds, " there is nothing special in the facts, except the " apparently large amount of gastric affections prevalent in Gibraltar " at all times, and the probable influence of this state of health in pre- " disposing people to attacks of cholera during epidemic seasons " (p. 2). Inspector-General Rutherford, M.D., writing of the state of public health in Gibraltar in 1865, previous to the appearance of the epidemic there, says, " The summer of 1865 in Gibraltar, up to the " time when cholera first appeared, viz., 18th July, was regarded as " unusually cool and agreeable, and the somewhat exceptional good " health of the inhabitants was a subject for congratulation."†

The absence of all fore-shadowing of the epidemic at Gibraltar, can hardly be reconciled with the suggested presence of such fore-shadowing at Malta. The facts which have been interpreted as presaging the appearance of cholera in the latter island, are, indeed, to be regarded rather as coincidental than precursory.

Again, MM. Didiot and Gués have endeavoured to show that prior *in Marseille.* to the appearance of cholera in Alexandria choleraic disease existed in Marseille, and that the outbreak of the epidemic in the latter town was preceded by " une constitution médicale cholérique."‡ The facts they

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* Return showing the Number of Cases of certain kinds of Sickness under observation during the first six months of 1864, and during the corresponding period of 1865, at the Civil Hospital, Gibraltar :—

Months—January to July inclusive.	1864.	1865.
Dyspepsia - - - -	446	420
Colic - - - -	268	231
Diarrhœa - - - -	252	239
Dysentery - - - -	47	26
Sickness and vomiting - -	116	181
All other diseases - - -	8,525	7,969

—*Report on the Epidemic of Cholera at Gibraltar in the year* 1865, p. 2.

† General Report upon the Cholera Epidemic in Gibraltar, during the Summer and Autumn of 1865.—*Statistical, Sanitary, and Medical Reports of the Army Medical Department*, Vol. vi., p. 350.

‡ *Rapports sur l'Origine du Choléra à Marseille en* 1865. Par Dr. P. A. Didiot and Dr. Ch. Gues, Marseille, 1866. " Le Dr. Didiot," writes Dr. Gués, " établit que " le choléra, dont l'éxistence officielle ne date, il est vrai, que du 23 Juillet, régnait " cependant à l'état sporadique depuis la fin du mois de Mai." (p. 26.)

advance in support of their conclusions simply show that deaths from infantile cholera, which, as they properly remark, is "à la vérité, "fréquente à Marseille," and from so-called "sporadic" cholera, are apt to occur in Marseille during the months of May and June, as in perhaps every city and town of southern and central Europe. Certainly they state that the cases of these diseases which occured in Marseille in May and June 1865 were characterised by unusual severity, but this statement is inconsistent with such facts as are known regarding the mortality from the malady. Dr. Seux, as the result of an examination of the registers of the Civil Hospital and of his own observation during the months of May and June, states: "Dans ce relevé, on ne rencontre "pas un seul cas de diarrhée aigué; dans la clinique de la ville, on "observait à cette époque le même genre de maladies qu'à l'hôpital; "les diarrhées, habituellement très fréquentes à l'arrivée des chaleurs, "l'étaient cette année moins que de coutume; en un mot, l'état "sanitaire de la ville était excellent." He adds also the following observations from data furnished to him by Dr. Jubiot, principal medical officer of the Military Hospital: "Durant les mois de Mai, Juin, et Juillet "1864, M. Jubiot a eu à soigner dans cet établissement 43 diarrhées; "tandis que durant les mêmes mois en 1865, il n'en a eu que 25 cas, ce "qui fait 18 cas de moins pour cette année. Il est donc évident que "dans le mois de Juin, Marseille se trouvait dans d'excellentes condi-"tions hygiéniques et sanitaires. Il est aussi parfaitement démontré, "par les détails qui précèdent, que la constitution médicale regnante "n'indiquait pas l'invasion prochaîne de choléra."* (p. 7.)

In England, although the introduction of Russian Steppe murrain early in 1865, after the country had been free from the epizöotic for a century, the threatenings of the rare malady epidemic cerebro-spinal meningitis prevalent at the beginning of the year in North Germany, and the unwonted appearance of relapsing fever during the winter in St. Petersburg had arrested public attention and excited the vigilance of the Government in the spring, it does not appear to have occurred to any-

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* Le Choléra dans les Hôpitaux Civils de Marseille pendant l'Épidémie de 1865. Par V. Seux, Médecin-en-Chef des Hôpitaux, &c. Paris, 1866.

Dr. Ménécier (*Histoire de l'Epidémie de Choléra à Marseille* 1865) gives the following statistics from the military hospital, furnished to him by Dr. Jubiot, and he precedes them with the observation:—"Les cas de diarrhée ont été si rares cette année, que le mot *diarrhée* n'a figuré qu'à partir du mois Août en tête de relevés d'observations météorologiques envoyés mensuellement au ministère de la guerre par l'hôpital militaire."

		1864.		1865.		
		Cases.	Deaths.	Cases.	Deaths.	
Diarrhœa	May	4	1	5	1	
	June	11	0	4	0	
	July	17	0	8	1	
Dysentery	May	2	0	4	1	
	June	6	0	4	0	
	July	1	1	8	1	
Cholerine	May	2	0	0	0	
	June	2	0	5	0	
	July	7	0	5	0	
Cholera	May	0	0	0	0	
	June	0	0	0	0	[18th June 1st case observed among civil population.]
	July	0	0	2	1	[23rd July officially recognized among civil population.]

one to see in these events presages of the extension of yellow-fever and of cholera to our shores later in the year. In fact the different occurrences were parts of contemporaneous rather than of successive phenomena.

The Antecedents of the Diffusion, 1865.

No notable change in the public health of the localities affected preceded the appearance in September either of yellow-fever at Swansea, as shown by Dr. Buchanan,* or of cholera at Southampton, as shown by Dr. Parkes.† Dr. Parkes submitted this question to very careful consideration, but neither in respect to meteorological states nor in respect to sickness among the population was he able to detect the existence of any peculiar "epidemic constitution", so-called, preceding or co-existing with the cholera. Taking the mortality from diarrhœa as the best indication of the operation of any generally existing cause favouring the production of cholera, he found that the annual average number of deaths from diarrhœa in the district of Southampton during the four years 1861–64 was in September 12·75, and in October 2; and that in September 1865, the deaths were 13, and in October 1865, when cholera was chiefly prevalent, they were only 7. In October 1864 the number had been 5. The inference from the records of mortality was confirmed by the information received from medical practitioners as to prevalence of diarrhœa, and Dr. Parkes observes: "Considering "then, that in the larger part of the town there was no excess of cases "of diarrhœa; that there was no increase in the deaths from diarrhœa "in September, and only an unimportant increase in October, and that "during a period of public alarm there are always persons who apply "for advice who in ordinary times would not think it necessary to do "so, I cannot believe that there is any evidence of a general diarrhœa-"producing cause hanging over Southampton."

in Southampton.

in Theydon Bois,

I made close inquiry as to diarrhœal antecedents in the outbreak of cholera at Theydon Bois, Essex, in September 1865, and I included other parishes of the Epping Union in the inquiry as well as the parish of Theydon Bois. The result proved that there had been no unusual prevalence of the disorder among the population, and that the cases which had occurred differed in no respect from those observed ordinarily in autumn. Two cases of common sporadic cholera had taken place in Epping, and several in the Haslow and Matchingham district about the time of the outbreak. But none of these cases proved fatal or presented any peculiar symptom. During the second week of the outbreak at Theydon Bois, there was an apparent prevalence of diarrhœa in that parish, arising from the energetic measures which had been taken in urging the population to apply for medical advice upon the occurrence of any, even the slightest, disturbance of the bowels.

and in London.

I further examined this question with reference to London, in my report on cholera in the Metropolis in 1866, especially in the eastern districts.‡ In that report I considered it first with regard to the prevalence of diarrhœa, as measured by the mortality registered under that term previous to the outbreak; and, next, with reference to reported cases of choleraic diarrhœa preceding it. In regard to diarrhœa, I discussed the question not only in respect to the outbreak of 1866, but also to the outbreaks of 1848–49 and 1853–54. From this discussion it followed that each epidemic of cholera since 1838 had been preceded

The prevalence of diarrhœa in 1866, in relation to Cholera, as observed in London.

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* *8th Report of the Medical Officer of the Privy Council*, p. 440.

† *Ditto.*

‡ *9th Report of the Medical Officer of the Privy Council*, p. 267, s. 4; and p. 217. s. 5.

by an excessive development of diarrhœa, but every excessive development of diarrhœa had not been accompanied by epidemic cholera. Thus in 1857, 1859, and 1861 the mortality from diarrhœa was unusually great. In the first-named year the deaths from the disease largely exceeded those from the same cause which preceded the epidemic of 1848–49. In 1859 the mortality from diarrhœa surpassed that which occurred during the second and principal year of the epidemic of 1853–54; and in 1861 the deaths from the same cause were in excess of those of the first year of the epidemic.

The absence of constant concurrence between years of excessive prevalence of diarrhœa and years of epidemic cholera was not the only point of deviation between the phenomena. When they occurred together the large amount of diarrhœa accompanying and developed during the progress of the epidemic did not merge insensibly into, or seem to arise directly and by steadily increasing augmentation out of, as a further exaggeration, the diarrhœa immediately preceding it. It appeared, indeed, to be a superadded phenomenon following a special law of increase and decline.

Immediately prior to the development of epidemic cholera in London in 1866 there was a remarkable subsidence of diarrhœa. A like phenomenon preceded the epidemics of 1848–49 and 1853–54. In the epidemic of 1866, the two first cases were recorded on the 26th June. The following table shows the mortality from diarrhœa during the four weeks of June and 1st week of July:—

Deaths from Diarrhœa.

	1865.	1866.	Average of corresponding Weeks, 10 years.
1st week June	44	22	18·9
2nd „ „	93	20	29·1
3rd „ „	187	43	48·8
4th „ „	184	67	58·7
1st week July	301	102	95·1

The little prevalence of diarrhœa in the metropolis immediately preceding the earliest cases of the epidemic in 1866, as indicated by the mortuary returns, was confirmed by an examination of the state of diarrhœa among the sick poor, during the months of May, June, and July, in the districts which suffered most from the outbreak.

Dating the actual commencement of the epidemic of 1848–49 from the 40th week of 1848, in the four preceding weeks, the 36th, 37th, 38th, and 39th, the mortality from diarrhœa had fallen markedly, and in the three latter weeks largely below the average. Dating also the active commencement of the epidemic of 1853–54 from the week in 1853 in which the deaths from cholera passed above the average, the 37th (the mortality from that time keeping persistently and conspicuously above the average to the close of the year), in the 31st, 32nd, and 34th weeks of that year the mortality from diarrhœa fell largely below the average of preceding years. A similar subsidence below the average did not occur, it is interesting to remark, in the corresponding weeks of 1854, or anterior to the recrudescence of the epidemic of that year. Subsequently to the outbreak of the epidemic of 1853, the weekly mortality from diarrhœa kept steadily above the average of the preceding three years until the recommencement of the activity of cholera in 1854. The mortality fell to a lower point during the period from the 26th to

the 27th week inclusive, but always kept above the average. In the last week of the period the epidemic again became active, and subsequently the mortality from diarrhœa rose and sunk, with its development and declension.

Deaths from Diarrhœa.

Week of Year.	1848.	Average of corresponding Weeks, 5 years.
33rd	81	66
34th	63	66
35th	79	66
36th	61	66
37th	42	66
38th	46	66
39th	44	66
40th	47	21

Week of Year.	1853.	1854.	Average of corresponding Weeks, 3 years, 1850-52.
30th	81	84	70·1
31st	110	142	134·2
32nd	139	195	167·0
33rd	126	192	165·1
34th	137	214	156·1
35th	152	243	139·0
36th	131	276	124·0

I argued from the foregoing data that there was no essential etiological connection between the diarrhœa which preceded and the diarrhœa which accompanied (and was, in fact, a part of) the epidemic of cholera in 1866, and the two previous epidemics. The diarrhœa which accompanied the epidemic of 1866 sprang up contemporaneously with the first cases of cholera, grew in extent with the growth of the epidemic, and diminished with its decline; and probably was altogether independent of, although associated with the current sporadic diarrhœa of the country.*

* Dr. Edward Ballard makes the following observations on diarrhœa observed in Islington during 1866, in his "Report of the Results of an Analysis of Records of Sickness kept in Islington during the 12 years, 1857 to 1868 inclusive."—(*11th Report of the Medical Officer of the Privy Council.*)

"The exceptional cholera year 1866 deserves particular notice, chiefly because the summer diarrhœa, the recorded cases of which amounted in the three months, July, August, and September, to 1,879, did not correspond to the meteorological conditions existent during its prevalence, neither did the summit of the diarrhœal wave correspond with that of the wave of epidemic cholera as it presented itself in this district. The mean temperature of the 13 weeks of summer was positively low, viz.:—58·7°, that of the four weeks of July being 61·5°, of the four weeks of August 58·9°, and of the five weeks of September 56·9°. The humidity of the atmosphere also was great for the season, and the rainfall considerable. It was therefore impossible to fail in recognising in this season the operation of a cause other than the ordinary meteorological causes of summer diarrhœa, producing the enormous amount of diarrhœa observed:—for the cases recorded upon the books, numerous as they are, did not represent anything like all that were admitted under treatment. A consideration of the temperature of the season week by week will put this in a still clearer light. In the fourth week of June the mean temperature was 58·1°, and in the fifth week it suddenly rose to 66·3°, in the week following it fell 10·0°, to rise in the second

The prevalence of diarrhœa in relation to cholera in England and Wales.

THE ANTECEDENTS OF THE DIFFUSION, 1865.

I have since examined the relationship of the mortality from diarrhœa to that of cholera, in England and Wales, during the past 20 years, 1847–67. This period includes the three epidemics of 1848–49, 1853–54, and 1866. The results correspond so closely with those obtained by the examination of the like relationship in the metropolis, that it is unnecessary to describe them in detail, and I give the annual figures in the Appendix (Table I.). Since 1867 there has been a considerable growth in the mortality from diarrhœa, and in 1868 the numbers of deaths registered from this cause in England and Wales exceeded, as well in gross number as in proportion to population, those of any previous years. The mortality from diarrhœa in 1865 was, in England and Wales, 28,531, the greatest number recorded to that time in any year since the establishment of registration. In 1868 the number of deaths from diarrhœa in England and Wales was 29,821. Moreover, in 1870 and 1871, the deaths from diarrhœa proportionately to population had, with the exception of 1868, been exceeded in three years only of the period under consideration, namely, in 1854, (when cholera was epidemic), in 1857, and in 1866. The deaths from diarrhœa registered in the two years respectively were 25,311 and 24,140. These later great developments of diarrhœa presaged no epidemic of cholera, and they appear to confirm the conclusion arrived at from the examination of the data relating to the metropolis, that the diarrhœa of ordinary seasons and the diarrhœa accompanying epidemics of cholera are phenomena determined by a different series of causes having no etiological relations except such as are secondary.

Preceding the outbreak of cholera in the metropolis in June 1866, several deaths from "choleraic-diarrhœa," and one certified as from "Asiatic cholera," had been registered. Three of these cases had occurred in April, and seven, including the case of so-called "Asiatic cholera," in May. In 1865 also, deaths from "choleraic-diarrhœa" and from so-called "Asiatic cholera" had been registered, the earliest (deaths from the first-named malady) in the week ending the 22nd July. Of these cases I wrote at the time, "It is not easy to assign a determinate value to the term " 'choleraic-diarrhœa.' As a cause of death it has for some time appeared " annually in the weekly returns of the metropolis. . . . . On any " view of the probable relations of these cases to the subsequent " epidemic it is requisite that they should be noted. It is found im- " possible to disentangle at the beginning of the outbreak cases of a " quasi-epidemic character from those of a true epidemic character, and " to shut out absolutely a theory of development of the latter by grada- " tion out of the former; it is equally impossible to set aside the fact of " exposure of the metropolis to continuous transmission of the epidemic " malady from the early autumn of 1865 to the early summer of 1866. " The history of the outbreak, where defective, as here, must be com- " pleted by deductions drawn from the history of the general epidemic

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week of July 12·0°, to 68·2°, the highest weekly mean of the year. For four or five weeks after this it progressively fell to 58·0°. The month of June was not remarkable for diarrhœa, and gave no promise, had not cholera been anticipated, of a heavy diarrhœal epidemic. In the fifth week of June only 28 cases were recorded; in the first week of July there were 55 cases, and they increased week by week thus: 43, 99, 115, 165, 272, 313, the last number being attained the third week of August, that is five weeks after the maximum temperature had been reached, the steady increase of cases having gone on concurrently with a steady decline of mean temperature below 60·0°. Our maximum of weekly cases of diarrhœa was attained on the second week after the first fatal week of cholera in London, which was also the week in which the largest number of cases of the disease was observed in Islington. Diarrhœa then increased as cholera declined."—(pp. 51 and 54.)

" of which it forms a part." * Since this was written I have had to give particular attention, as part of my official duties, to cases of diarrhœa and choleraic disease of a quasi-epidemic character, in view of threatened extensions of the true epidemic disease. As the result of several investigations it has appeared to me that very much of the difficulty here arises rather from phraseology than from fact. A tendency has grown up during the recurring epidemics of cholera to apply the terms proper to the period of epidemic prevalence to sporadic forms of the disease, as if fatal cholera and fatal serous diarrhœa were diseases unknown to England prior to the intrusion of Asiatic cholera. This looseness of phraseology is to be deprecated, as still further complicating an otherwise very complicated subject. With regard to the question now under consideration, namely, the significance of these cases as presaging epidemic cholera, I have failed to discover any closer relation between their occurrence and the appearance of epidemics of cholera than that which exists in respect to common diarrhœa.†

I have examined the question under consideration with reference also to the prevalence of "fevers," and generally of zymotic diseases previous to the appearance of epidemics of cholera in this country. I give the data in the Appendix (Table I.). They do not appear to me, any more than the data derived from the mortality from diarrhœa, to yield evidence of a so-called "epidemic constitution" foreshadowing the different invasions of the pestilence.

The Diffusion.—On the 2nd June 1865 the first observed case of cholera occurred in Alexandria. On the 11th June the presence of the disease in the city was officially recognized. On the 12th June, in consequence of the appearance of cholera, the issue of foul bills of health to ships leaving the port began. The Italian steam vessel, "Principe di Carignano," which started for Ancona that day, had inscribed upon its bill of health, "Quelques cas de cholera ont été observé "à Alexandrie du 10 au 12 juin present mois." On the 14th June the appearance of cholera at Alexandria was made known through the telegraph to the different maritime nations of Europe by their representatives there.

The Diffusion from Alexandria to Europe.

The dates of the subsequent appearances in the Mediterranean and in Europe, together with the dates of such appearances elsewhere, as it is desirable to note for the purpose of marking contemporary diffusion, are given in the following list. Places not in Europe are printed in italics :—

June 18th. Marseille (officially recognized 23rd July).
„ 20th. Malta.
„ 24th. *Smyrna.*
„ 28th. Constantinople.

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* *9th Report of the Medical Officer of Privy Council*, p. 272.

† If I may trust to my own experience, commencing with the epidemic of 1848–49, the term "choleraic-diarrhœa" has come into common use since the epidemic of 1854. The instructions as to returns of cases prepared in that year by the Committee for Scientific Inquiries of the General Board of Health, directed that "the "following *degrees or stages of the disease* should, where possible, be distinguished," namely (1) "simple diarrhœa," (2) "choleraic-diarrhœa," and (3) "cholera." "Choleraic-diarrhœa" was described thus: "Alvine discharges very copious, watery, "still tinged with bile. Vomiting generally present, but not continued or urgent. "Cramps absent." Choleraic-diarrhœa here meant a form of malignant cholera, and in this sense the term is adopted in the nomenclature of the Royal College of Physicians; but it has become a too common practice to apply it now to forms of sporadic diarrhœa, which in certain aspects are like unto cholera.

July	1st.	*Beyrout*, city (29th June, lazaretto).
„	„	*Jaffa.*
„	7th.	*Cyprus* (Larnaka, town : lazaretto, 26th June).
„	„	Ancona.
„	8th.	Valencia.
„	„	*Dardanelles*, town (29th June, lazaretto.)
„	18th.	Gibraltar.
Aug.	1st.	*Damascus.*
„	„	*Trebizond*, town (25th July, lazaretto).
„	2nd.	Sulina, town (30th July, lazaretto).
„	„	Kustendji.
„	4th	Tultcha.
„	9th.	Novorossiisk (Caucasia).
„	10th.	Borchi (district of Balta, Government of Podolia, South Russia).
„	„	Odessa, lazaretto (18th officially recognized in the town).
„	11th.	*Aleppo* (officially declared).
„	19th.	Palma.
„	22nd.	*Erzerum.*
„	27th.	Altenburg (Saxony).
„	29th.	Kertch.
Sept.	4th.	*Algiers.*
„	17th.	*Bagdad.*
„	„	England : Southampton.
„	18th.	Paris (Puteaux).
„	28th.	San Giovanni à Teduccio (near Naples).
„	29th.	Prosecco (near Trieste).
Oct.	6th.	Naples.
„	22nd.	*Guadeloupe.*
„	28th.	Taganrog.
Nov.	22nd.	*Ward's Island, New York* (quarantine station, Lower Bay, 2nd November).

The relation of the several appearances in Europe to the outbreak at Alexandria, or to each other, is given in the following details :—

The appearance at Marseille, 18 June 1865.

Marseille.—On the 11th June the steam-ship "Stella" entered the harbour, having sailed from Alexandria on the 1st of the month. She landed 97 passengers, of whom 65 were Algerian pilgrims returning from Mecca, and according to M. Grimaud (de Caux), brought news of the existence of cholera in Alexandria.* On the evening of the 11th June the "Byzantine" arrived with 55 passengers. She had sailed from Alexandria on the 3rd June, and touched at Malta on her voyage. On the 14th June the "Marie Louise" and the "Syria" arrived, the former bringing 21 passengers, the latter the English mail and 106 passengers. On the 15th the "Saïd" reached the port with 190 passengers, who were sent to Frioul under observation and were not landed at Marseille until the 17th. This was the first ship submitted to detention. On the 16th the "Volga" arrived with 29 passengers, who were disembarked at once. On the 18th came the "Montfaloux," and the "Nyanza," the former having left Alexandria on the 10th and

* *Gazette des Hôpitaux*, 17th Oct. 1865.

bringing five passengers, the latter having left Alexandria on the 11th and bringing 46 passengers. Both these ships were subjected to observation two days before the passengers and crew were allowed to communicate with the shore. After the 20th arrivals at Marseille from Alexandria were subjected to quarantine.

From the 9th to the 20th June 549 persons were landed at Marseille from Alexandria and dispersed in different directions, of whom 308 had undergone no observation.

The Algerine pilgrims, during their stay in Marseille (period not stated), were lodged under canvas in Fort Saint Jean. Sixty-seven pilgrims had sailed from Alexandria in the "Stella," but two had died on the eighth day of the voyage. A third pilgrim died about five hours after landing at Marseille. The death of the latter was attributed, on insufficient evidence, to chronic dysentery; the deaths at sea are stated in the Report of the International Sanitary Conference, 1866,* to have been caused by cholera. Several of the pilgrims were indisposed at the time of landing.

While the pilgrims remained at Marseille they were an object of much curiosity to the frequenters of the quays. Many flocked to witness their appearance and habits, and they themselves moved freely about the streets in the vicinity of their temporary quarters.†

Two deaths from cholera occurred on board the "Saïd" in the course of her voyage from Alexandria, and on the 17th June, the day her passengers were disembarked at Marseille, Dr. Seux was summoned to one of them, a Jewish lady, suffering from diarrhœa which he considered to be choleraic. He saw other cases of a like nature on following days among fugitives from the epidemic at Alexandria. On the 18th June a well-marked case of malignant cholera occurred under the observation of Dr. Aïdé, the patient being a woman, aged 38 years of age, having charge of an infant, the child of a stoker on board a steam-vessel then in the port, and through whom she had frequent relations with the port. Other marked cases are recorded by Dr. Seux as happening during the remainder of the month of June and the beginning of July, and from the 23rd of that month it became no longer possible to shut the eyes to the fact that cholera was widely scattered in the city.‡ Nineteen cases were recorded in the nine days, 23–31 July, and the probable source of these was made a subject of careful inquiry by Dr. Ménécier. Of two of the patients no history could be obtained, but all the remainder, several of them being sailors and others workmen in the Imperial Mail Steam-Packet Service, were connected more or less closely with the port and the shipping.§

After the 23rd July the epidemic in Marseille slowly increased until the middle of September, after which period it declined, ending before the close of December. From the commencement on the 18th June, 1,952 deaths from cholera were registered. During the course of the

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* *Rapport sur la Marche*, &c., p. 52.

† "Pendant quelques jours, la horde des pélerins Arabes a, comme toujours, excité par sa malpropreté, par ses habitudes singulières, la curiosité des habitants des quais, et, comme toujours, soit qu'ils fussent allongés sur les dalles, soit qu'ils prissent leur dégoûtante nourriture, soit enfin qu'on les vit acheter à vil prix, ou ramasser dans les rues les rendus des marchés, une foule assez nombreuse entourait les sectaires de Mahomet."—*Étude sur le Choléra de Marseille en* 1865. Par Drs. J. Laugier et C. Ollive, Médécins des Bureaux de Secours, &c. Marseille, 1865, p. 20.

‡ *Le Choléra dans les Hopitaux Civils de Marseille*, 1865, p.p. 2–3 and 9–11.

§ *Historique de L'Epidémie de Choléra à Marseille*, 1865, p. 11, et seq.

epidemic several of the ships arriving from Alexandria in the port had had deaths from cholera on board.*

The appearance at Malta, 20 June 1865.

Malta.—The first case of cholera occurred in Malta (Valetta) on the 20th June.

On the 31st May the British steam-vessel "Ephesus," which had left Alexandria on the 26th May, arrived in the harbour of Valetta, with 235 pilgrims returning from Mecca on board, and was admitted to pratique. The next day she sailed for Tunis leaving 61 of the pilgrims at Malta. The master reported that during the voyage from Alexandria three pilgrims had died, one from "sore-leg," another from "costiveness," and the third from "senile exhaustion."† From the 1st to the 14th June inclusive, 14 steamers from Alexandria (the last arriving having sailed from Alexandria on the 9th June) touched at Valetta, and several landed passengers. Some of these vessels also carried pilgrims returning from Mecca. On the 14th the first news of cholera having broken out at Alexandria reached Malta; and on the evening of the same day quarantine was put in operation against vessels coming from that port. From the date of arrival of the first body of pilgrims in the "Ephesus" on the 31st May to the adoption of quarantine on the 14th June, 845 passengers had been brought into the port of Valetta from Alexandria, of whom 426 were pilgrims. Nearly all these persons landed during the stay of the vessels in the port, and several‡ were passengers for Malta.

Of the persons destined for Malta, of the persons who landed and remained there several days, including the 61 pilgrims, and of the persons who merely went ashore during the stay of their vessel in the harbour (of the latter almost necessarily), nothing whatever appears to have been ascertained as to their state of health at the time of and subsequent to landing.

The passengers first subjected to quarantine, 76 in number, of whom 51 were pilgrims, were landed at the lazaretto on the evening of the 14th June from three ships, the "Memnon," "the Cairo," and the "Nyanza." The "Memnon" carried 133 pilgrims from Alexandria, the majority for Tangiers. One pilgrim had died on the voyage from "bowel complaint." Fourteen pilgrims were landed at the lazaretto and 22 other passengers. The "Cairo" landed 47 passengers, 37 being pilgrims; and the "Nyanza" 7 passengers. On the 17th and 19th two steamers arrived at Malta from Alexandria, one of which landed at the lazaretto 30 passengers, the other one passenger. On the 20th June the steam vessel "Rhone," also from the same port, entered the harbour, with 147 passengers for Malta. The master reported that a passenger and a fireman had died from cholera during the voyage. On the 23rd one of the passengers landed from the "Rhone" was attacked with sickness and vomiting, and on the following day, the 24th, two other passengers, landed from the same ship, were attacked with diarrhœa. On the 23rd a man, landed from a ship, "the Christine," the day before, had also been attacked with diarrhœa. On the 26th of June there was another case of diarrhœa and vomiting in the lazaretto, the person having been landed there on the 23rd. None of these cases were fatal.

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* Thus, the *Tarifa*, 1 death; the *Vincent*, 1; the *Copernic*, 1; the *Cella*, 1; the *Asia*, 2; the *Saïd* (a second time), 2; the *Marie-Louise*, 3; the *Brésil*, 1; the *Oronte*, 1; the *Byzantin*, 1.

† *See* Dr. Ghio's Report, p. 11. Dr. Sutherland states as to the first-named cause of death, "mortification," not "sore-leg." (Report, p. 16.)

‡ Thirty-six, according to Dr. Sutherland. (Report, p. 16.)

On the 28th June the steamer "Wyvern," of 586 tons burden, five days out from Alexandria, landed 302 passengers at the lazaretto, and among them two cases of cholera. One of these cases died on the jetty, the other recovered in the quarantine hospital. In the course of the evening of the 28th a passenger, landed from the "Wyvern," was attacked with cholera in the lazaretto. These were the first cases of cholera in the lazaretto. Other cases followed among the passengers landed from the "Wyvern," not less than 11 occurring, with two cases of severe diarrhœa, and eight deaths, from the 28th June to the 17th July.

The first case of cholera among the population of the island, as already stated, occurred on the 20th June. On that day a child of one of the families of a detachment of Royal Artillery stationed in the former "Plague hospital," on Lazaretto Island, was seized with cramps, diarrhœa, and vomiting, and died after eight hours illness. This case is held to be the beginning of the outbreak in the island.

The quarters of the "Plague hospital" were described at the time as situated between two burial grounds, and surrounded by a wall 15 feet high. They were close, ill-drained, and near to the stagnant, foul-smelling shore of the Lazaretto creek. The inmates had been affected more or less with diarrhœa "for some time previously."

On the 22nd June a woman in the same quarters died after 18 hours illness, characterised by diarrhœa, vomiting, and cramps.

The day following (the 23rd) another woman, the mother of the child first attacked, was seized with similar symptoms and died after three days illness.

Four days afterwards (27th June) a second child died with choleraic symptoms.

During the night of the 27th–28th a workman (a civilian), who had been employed in lime-washing some rooms at the "plague hospital," was attacked with cholera at Casal Attard, and died on the 29th. This was the first known case among the civil population of Malta.

On the 1st July the detachment of Artillery was removed from the "Plague hospital" to the Salvatore Counter-Guard, beyond Floriana Parade, and near the Hay Wharf. The same day, after the detachment had taken up its quarters in this counter-guard, five of the soldiers' wives became ill, three suffering from decided cholera. The nature of two of the cases was doubtful. Of the three marked cases one died in 26 hours.

On the 3rd July a woman who had attended the last-mentioned fatal case, but who had not lived at the "Plague hospital," was seized with cholera after neglected diarrhœa of three days standing. She lived five days.

The same day the first case took place, at No. 96 Strada Vescovo, among the civil population of Valetta.

From this date the disease began to extend over the city and island.

Gozo.—The appearance of the disease in the island of Gozo is thus described by Dr. Ghio:—

"The island of Gozo, which lies at a distance of about three miles to the west of Malta, remained free from the disease till the 21st July. On that day Michele Cilia, aged 22 years, a seaman employed in a coasting boat, returned to Gozo after nine days stay at Malta. He arrived at Casal Xeuchia, the place of his residence, at about 3 p.m., suffering from diarrhœa. During the ensuing night he was seized with cholera, but recovered.

"On the 12th July, four cases occurred in two sisters of the said

Michele Cilia and two female neighbours who had frequented the house of Cilia during his illness.

"On the 25th, two other attacks followed among the inhabitants of the same Casal, one of whom also visited Cilia's house. After that day several other attacks took place.

"On the 2nd of August, the disease appeared in other Casals of that small island."*

The following Table shows the sickness and mortality caused by cholera in the two islands during the epidemic:—

—	Population.	Duration of Epidemic.	Cholera.	
			Cases.	Deaths.
	Civil.	1865.		
Malta - - -	(1861) 118,596	28 June—9 Nov. -	2,362	1,479
Gozo - - -	„ 15,348	21 July—24 Oct. -	545	252
	Military.			
Garrison:—	(Average.)			
Men - 6,105	7,469	20 June—12 Nov.	199	142
Women - 526				
Children - 838				
Lazaretto - -	—	—	—	—
Health Guards 134				
In communication with - 138				
Passed through quarantine, 14 June to 31 July - 2,031	2,303	23 June—29 July	23	14

The appearance at Constantinople, 28 June 1865.

Constantinople.—On the 28th June, at a time when, according to the Report of the International Sanitary Conference of 1866, "ni le choléra "ni rien de ce qui ressemble à ce qu'on appelle les signes précurseurs "de cette maladie, n'existaient à Constantinople," the Ottoman frigate, the "Mukbiri Surar" arrived in the Golden Horn from Alexandria, having left the latter port on the 21st. A declaration had been made that neither deaths nor sickness had occurred on board during the voyage, and in accordance with a quarantine regulation which exempts from detention vessels which have been five days at sea without the appearance of choleraic disease, and which carry a medical officer, she was at once admitted to free pratique. The evening of the ship's arrival, 12 sailors were sent from her into the Imperial Marine Hospital, 11 suffering from choleraic diarrhœa, and one from cholera. The case of cholera ended fatally in the course of the night. On the 30th June, seven other cases of choleraic diarrhœa and two cases of cholera were disembarked and sent into hospital. It was subsequently ascertained that diarrhœa had existed among the crew when the ship left Alexandria, and that two sailors had died from cholera, the corpses being cast overboard, while the vessel was traversing the Sea of Marmora. On the 5th July cholera broke out in the arsenal, within the precincts of which the hospital lies, first in the barracks through which the sick were carried from the frigate to the hospital, and next among the labourers in the workshops. From the 5th to the 15th July there

* Report, p. 14.

occurred in the barracks, among the workshops, and on board the ships lying off the arsenal, 71 attacks and 26 deaths. On the 9th the disease appeared in the suburb adjoining the arsenal, the earliest cases taking place among labourers living there engaged in the arsenal. Subsequently cholera appeared in and extended throughout the various quarters of the city. An instructive episode of this outbreak is related as follows :— On the 11th July a workman left the vicinity of the arsenal and visited the village of Yeni-Keni, several miles from Constantinople, on the west shore of the Bosphorus. The same evening he was seized with cholera while at a café. On the 12th July, the day following, several Mahommedan labourers and Greek boatmen who visited the same café were attacked with diarrhœa. This was the commencement of a disastrous outbreak in Yeni-Keni and the vicinity.

The appearance at Ancona, 7 July 1865.

Ancona.—The first authenticated case of cholera occurred in this port on the 7th July, but there appear to have been suspicions of the existence of the disease there before that date. The *Lombardy Medical Gazette* attributed at the time the introduction of the disease to the steam-ship "Principe di Carignano," coming from Alexandria, which as already stated, was, on the 12th June, the first to receive a foul bill of health on leaving that port. This ship arrived at Ancona on the 17th June, carrying 60 passengers, and was subjected to seven days quarantine. All ships arriving from Alexandria were afterwards placed in quarantine, for the same or a longer period of time, until the end of the outbreak in Lower Egypt. Persons detained in the lazaretto would appear to have had the privilege of sending their linen into the town to be washed, for it is to this custom, and especially to the washing of linen belonging to invalids from Alexandria then under detention, that the case of the 7th July is attributed in the Report of the International Sanitary Conference of 1866. The evidence upon this subject, however, so far as it has come under my observation, simply goes to prove that the quarantine was illusive. The mode in which cholera was introduced into Pistoia indicates the probable mode of its introduction into Ancona, and was thus stated in an official despatch of Her Majesty's Chargé d'Affairs, Florence, dated the 15th July 1865 :—"A woman who arrived from Alexandria at Ancona "on the 3rd inst. remained at the lazaretto of that place, in con- "formity with quarantine regulations, for the space of six days. She "left the lazaretto on the 9th, was taken ill on the 10th, while travel- "ling towards Pistoia, where she died on the following day with all "the known symptoms of Asiatic cholera."

This case and that of the 7th July in Ancona were the ascertained beginnings of the epidemic in Italy.

The appearance at Valencia, 8 July 1865.

Valencia.—On the 8th July a French merchant named Honoré Teissier was seized with fatal cholera immediately after his arrival at a boarding-house in the Fisherman's-Ward district (El Barrio de Pescadores). This was the first case of the epidemic in Spain. The merchant had come from Alexandria by way of Marseille, landing at Grao, the port of Valencia. Cholera had then been growing for nearly a month in Marseille, but was not officially recognised there until the 23rd July. Other inmates of the boarding-house were next attacked ; then inmates of houses in the neighbourhood. Some of the early cases were taken to the general hospital, and after their admission several patients, already under treatment in the wards, were attacked with cholera. The disease extended throughout the city, killing, from the 8th July to the close of September, 3,551 persons out of 8,800 attacked, among a population estimated at 107,000, but diminished by flight 40,000 during the prevalence of the epidemic.

The appearance at Gibraltar, 18 July 1865.

Gibraltar.—I take the facts of the appearance of the epidemic here from Dr. Sutherland's report.

On the 6th July 1865 the steam transport "Orontes" left Malta (Valetta) for Gibraltar, having on board the 2nd battalion of the 22nd regiment, destined for Mauritius, together with invalids and time-expired men, besides women and children. Cholera, as stated in a previous section, had appeared among the garrison of Malta on the 20th June, and among the civil population of Valetta on the 28th. On the 10th July, after a voyage of four days, the ship arrived at Gibraltar, and the battalion was landed and marched to the usual camping ground on the North Front, outside the fortress, at a distance of 1,000 yards and upwards from the walls, the invalids, time-expired men, and some of the women and children remaining on board the "Orontes."

"With the exception of a single trifling case of diarrhœa, the regiment remained in perfect health after landing until the 18th, when a private, named Bird, presented himself to the medical officer about 9 o'clock at night, labouring under cholera, of which he died about half-past 10 the following morning. It is not known whether this man had had any previous diarrhœa, but he was at parade at 7 o'clock in the evening of the same day, or two hours before he was seized with cholera. This was the first case of the Gibraltar epidemic of 1865."

The camp was at once broken up, the head-quarters being embarked on the transport "Star of India," at anchor in the bay, and the 2nd wing moved to a new camping ground on the east side of the North Front, close to the Mediterranean, and 400 yards further away from the garrison. These movements were all completed on the 19th. The "Star of India" was detained in the bay 48 hours, when, all seeming well on board, she was allowed to go to sea. During the voyage to Mauritius five cases of diarrhœa were recorded among the soldiers, all of which recovered, but no case of cholera.

Two cases of diarrhœa occurred among the men of the 2nd wing of the 22nd after its removal to the new camping ground, but otherwise the health of the soldiers remained good until the 31st July. On this day a man named Davis, of intemperate habits, and who had been complaining for two days of indisposition, was attacked with cholera at 11 o'clock a.m., and died at 8 o'clock the same evening. The next day the wing was embarked on the transport "Davenport," and after 60 hours detention the vessel was sent to sea. Two of the men were suffering from diarrhœa at the time of embarkation, and two other men had diarrhœa during the voyage to Mauritius. All the cases recovered. The "Orontes," which had brought the battalion from Malta, sailed for England on the 14th July with 223 time-expired men, invalids, and women and children on board, and after a six days voyage she reached her destination without any new case of sickness having appeared in the ship.

On the 3rd August a corporal of the 15th regiment, occupying, with his family, a cottage under the North Front, 800 yards distant from the camp vacated by the 2nd wing of the 22nd regiment on the 31st July, was seized with cholera, together with one of his children, aged four years. The father died in 48 hours, and the child in 15 hours. A third case, which recovered, occurred in another child of this family (date not recorded).

On the 9th August a woman belonging to the Royal Engineers, inhabiting a cottage in the same locality, was attacked and died in 56 hours.

On the 10th August a soldier living in the Grand Casemates, within the fortifications of the northern extremity of the town, was seized with cholera and died in eight hours. During the afternoon and night of the

same day seven other soldiers were attacked, two of the cases being very severe, in the same barrack.

On the 10th, also, a civilian's child was suddenly seized with cholera on board a lighter in the harbour (of the Old Mole), and died there. This was the first case among the civil population.

On the 14th two cases occurred, one in a soldier inhabiting one of the cottages on the North Front, in others of which cases had taken place on the 3rd and the 9th; the other in a child of a civilian living in the south district of the Rock, on the other side of the town. On the 15th another soldier was attacked in the North Front cottages, and the next day two civilians were attacked, one at the limekiln, and the other at the slaughter-house on the North Front. The same day a child was attacked in the North Front quarters.

On the 18th another fatal case occurred in the Grand Casemates, and on the 19th the earliest cases, three in number, all fatal, took place among the civil population of the town. From this period the epidemic became general on the Rock, and continued until the 27th October, when the last case was recorded. The following is a return of the cases and deaths from cholera during the prevalence of the disease :—

—	Population	Cases.	Deaths.
Civil - - -	17,491	902	747
Military (including the families of the garrison).	5,978	163	106
Convicts - - -	850	79	54
Totals - -	24,319	1,144	637

The appearance in South Russia. Borchi, 10 Aug. 1865.

Borchi and *Odessa.**—Borchi is a village in the district of Balta, government of Podolia, South Russia. On the $\frac{\text{O.S. 26 July}}{\text{N.S. 7 August}}$ 1865 several German families arrived there for employment on railway works in the vicinity. All appeared in excellent health when they reached Borchi, except an infant belonging to a family named Jans, which was suffering from diarrhœa. This infant died on the $\frac{29 \text{ July}}{10 \text{ August}}$. On the $\frac{1}{13}$th August cholera appeared among the inhabitants of the village. On the $\frac{6}{18}$th the mother of the infant Jans and two infants in other of the German families were attacked. All died, the woman on the $\frac{8}{20}$th. On the $\frac{7}{19}$th the wife of a man named Glenberg was seized with cholera. She died 12 days after in the stage of consecutive fever. On the $\frac{12}{24}$th William Exenberg was attacked; he recovered after a fortnight's illness. On the 21st the son of Glenberg was attacked and died the same day. Altogether eight of the Germans suffered from cholera, of whom one only recovered.

The progress of the disease among the inhabitants of the village during the above period has not been reported. These numbered 558, and among them, before the epidemic ceased, there were 65 cases of cholera, 33 of them fatal.

On the $\frac{25 \text{ August}}{6 \text{ September}}$, while cholera was still prevalent in the village, a church festival took place to which came several persons from Gavinossa, a neighbouring village having a population of 444. These

* In all Russian and Rumanian references as to date, it is to be remembered that they are expressed in so-called "Old Style," dating 12 days behind the "New "Style" Calendar, which is in use in Western Europe. In the text of this report, except otherwise stated, both styles are expressed; but in the Tables given in the Appendix the "Old Style" only.

THE DIFFUSION TO EUROPE, 1865.

persons on their return home, the same day, were attacked with cholera. The disease next appeared among the other inhabitants of Gavinossa, 37 cases and 22 deaths occurring.

Afterwards other localities in the district were attacked by cholera.

The series of events here described formed the first obvious manifestation of the epidemic in Russia, and it was believed to have been started by the German families, or rather by the sick child which they had brought with them to Borchi. These families had travelled by way of Galatz and Odessa,* being at Galatz on the $\frac{23 \text{ July}}{4 \text{ August}}$, and at Odessa, on the $\frac{24 \text{ July}}{5 \text{ August}}$, reaching Borchi, as already stated, on the $\frac{26 \text{ July}}{7 \text{ August}}$. The first recorded cases of cholera on the Danube occurred at Sulina on the 30th July, and at Tultcha on the 4th August. The appearance of the disease in Galatz was officially recognised on the $\frac{24 \text{ July}}{5 \text{ August}}$, and in Odessa, on the $\frac{29 \text{ July}}{10 \text{ August}}$ in the lazaretto, and in the town on the $\frac{6}{18}$ August. The history of the appearance of the epidemic in the last-mentioned town is as follows :—

Odessa, 18 *August* 1865.

Odessa.—From the $\frac{29 \text{ July}}{10 \text{ August}}$ cases presenting all the symptoms of epidemic cholera were received into the lazaretto of this port from vessels of various kinds which arrived from Constantinople. On the $\frac{5}{17}$ August a Customs' officer, named Gouline, on duty in the quarantine harbour, became indisposed and was relieved from duty and sent to his lodgings, Slobodka Voronzow, near Moldavanka. The next day, the $\frac{6}{18}$th August, his illness was recognised to be cholera, and he was removed to the city hospital, where he died an hour after admission. Two days after the death of Gouline, his wife, son, and servant were attacked with cholera, and the last-mentioned died.

On the $\frac{22 \text{ August}}{3 \text{ September}}$ two labourers working in the quarantine harbour, one of them a Jew, named Dorfmann, living in Jew's Street, were attacked with cholera. At the same time the wife of the porter of the house next to that in which Dorfmann lodged fell ill from cholera. On the $\frac{23 \text{ August}}{4 \text{ September}}$ her husband was also attacked, and on the $\frac{24 \text{ August}}{5 \text{ September}}$ their daughter. Of these cases Dorfmann alone recovered.

On the $\frac{23 \text{ August}}{4 \text{ September}}$ Borchinsky, a labourer also employed in the quarantine harbour, was attacked on his way homewards to Ouspenski Street, and he died the following morning. The same day his son, aged two years, and his daughter, aged six months, succumbed to the disease. Two days after his widow was attacked, and she died the second day.

In Ouspenski Street and the suburb Moldavanka the majority of the cases in Odessa occurred (236 to the $\frac{14}{26}$th September, of which 109 died). Elsewhere in the city the number was insignificant.

The German families bound for Borchi were at Galatz the day preceding the official recognition of the presence of cholera in that town, and they passed thence down the Danube the day the disease

* The fact of the families passing through Odessa is not mentioned either in Dr. Arkhangelsky's recent work on cholera in European Russia (*Epidemics of Cholera in European Russia during the* 50 *years* 1823–72); by Dr. G. T. Arkhangelsky, St. Petersburg, 1874 (Kholerina Epidemiu v Europeiskoi Rossi, v 50ti. letnei period 1823–1872); or in the Report of the International Sanitary Conference of 1866 "*Sur la Marche*," &c. It is stated, however, in the report of the Conference "*Sur les questions du programme relatives à l'Origine, à l'endémicité*, &c., *du cholera*" (p. 2), and in an official report of the outbreak, published in the "Journal de St. Petersbourg" for the 14th–26th Dec. 1865. The families no doubt passed from Galatz to Odessa along the ordinary steamboat route by the Danube.

appeared at Tultcha, and five days after its appearance at Sulina reaching Odessa five days before the acknowledged commencement of importation of disease into the lazaretto there.* From the 5th July cholera had been rapidly extending in Constantinople. Of the value of the restrictive measures established at Odessa against arrivals from Constantinople, Dr. Arkhangelsky writes, in the work previously referred to :—"The quarantined were not entirely isolated from commu- "nications with the inhabitants, and the transfer of cholera was as easy "as if no quarantine existed." The same observation is equally applicable to the quarantine established at Galatz, Tultcha, and Sulina.

The appearance at Sulina, 30 July 1865.

Sulina.—On the 30th July 1865 an Ottoman steam transport arrived in the roadstead of Sulina from Constantinople, having on board a crew for one of the iron-plated gun-boats in that harbour. The transport had lost two men from cholera during the voyage. The gun-boat crew was disembarked at once, several of the men suffering from choleraic symptoms at the time, and all were quartered in an isolated building. There during that and the following day (the 31st) 12 cases of cholera and five deaths from the disease occurred. On the 2nd August a labourer was observed by Dr. Jellinck, the medical officer in charge of the Navigation Hospital, ill of cholera among a body of labourers who had come from Galatz to Sulina, and who were encamped on the opposite side of the town from the lazaretto. The same day another case was discovered, the patient being a man employed in the Lieut.-Governor's office. From this date the disease spread in the town, and for the 20 days during which it lasted, among a population of 3,000, reduced half by flight, there were 350 cases, of which 300 died.

The appearance at Kustendji, 2 August 1865.

Kustendji.—On the 2nd August a person employed on the quarantine establishment was attacked with cholera and died. This was the first case of cholera recorded here, but towards the close of July certain attacks of so-called "bilious diarrhœa" had attracted attention. On the 4th August a quarantine guard and a blacksmith, an Englishman, were attacked with cholera ; the former died, the latter recovered. On the 5th another Englishman, a clerk of the quarantine establishment, and the son of the quarantine guard who had been attacked on the 4th, were seized with cholera, and all died. The disease then became prevalent in the town, and, out of a population of 4,000, killed altogether 120 persons. There were 20 cases and 11 deaths among 84 English residents.

The passengers landed in quarantine were sent to a temporary encampment two miles from the town, where they were detained three days. During the imposition of quarantine 95 ships, 28 being steam vessels, were subjected to it, and 1,508 passengers and sailors. Eleven cases of cholera occurred on ship-board, but none among the persons detained in the quarantine establishment. The dates of the cases on ship-board have not been stated.

Early in the outbreak of cholera at Kustendji several fatal cases occurred among the Bulgarian labourers employed in the town. Many thereupon fled to the mountains, and some to Rustchuk, where the disease first appeared among these fugitives.

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* In my report for 1865, the dates of the appearance of cholera at Borchi and Odessa, and of the passage of the German families along the Lower Danube and through the last-named town, were inadvertently given according to the Old Style, under the impression that the style had been changed in the French journal (*Journal de St. Petersbourg*, 14th-26th Dec., 1865) from which I obtained the facts. The same error (corrected by M. Fauvel in his work "*Le Choléra*") occurs in the Report of the International Sanitary Conference of 1866, on the progress of the epidemic, but not in the report of the Conference on the origin, endemicity &c., of cholera, where the introduction into Borchi is also described, the dates being here expressed in New Style. It will be observed that the alteration of the style removes the obscurity which rested upon the account of the introduction of cholera, in 1865, into Russia, as given in my first report.

The appearance at Tultcha, 4 August 1865.

Tultcha.—At Tultcha the disease was first recorded among a body of sailors sent from Constantinople to man certain ships of war in the river, and who had reached Tultcha on the 2nd August. From the 4th to the 15th August there were 14 cases and 10 deaths among these men. The disease next appeared among the civil population in communication with the ships of war, and among the marine soldiery. But the introduction of the disease into Tultcha is not attributed, in the Report of the International Sanitary Conference, 1866,* to the sailors, but to a body of soldiers who had arrived in the town previous to its appearance, and who had marched across the country from Constantinople. No history is given of this detachment or of its route.

From the 10th August to the 16th September 200 deaths from cholera, it is estimated, took place in the town, of which the population is said to be 20,000.

The appearance in Saxony, 27 August 1865.

Altenburg (Saxe-Altenburg, Saxony).—On the 27th August 1865, a woman, E., sickened of cholera in Altenburg, and died on the 29th, who had reached that town from Odessa on the 24th August. She had started on the 16th August, six days after the beginning of importation of cholera into the lazaretto of that port, and two days before the disease had been officially recognized as having appeared in the town; and she had with her a child, two years old, suffering from diarrhœa at the time of starting, and which still suffered when she reached her destination in Saxony. The journey occupied nine days and nine nights. The day E. died (the 29th), and in the same house, a sister-in-law was attacked with cholera in the evening and died on the 30th. The child was now removed by a sister of the woman E. to another part of the town, where it died from exhaustion on the 31st. These cases were the beginning of the epidemic in Central Europe.†

The appearance in England.

England.—Cholera appeared at Southampton in September, and a remarkable isolated outbreak of the disease occurred at the close of the same month and beginning of October, in the parish of Theydon Bois (Epping), Essex. In June a case of cholera, undistinguishable from the epidemic affection, was admitted into Guy's Hospital, in the Metropolis, under the care of Dr. Wilks. The patient recovered. On the 27th of the same month a second case, having all the characteristics of the epidemic affection, occurred in the Metropolis and ended fatally on the 28th. The patient was a water-side labourer, living in Wilmott's Buildings, St. George's parish, Southwark. If these cases belonged to the epidemic, and it is quite possible that they may have done so, as occurring within a period when London was exposed to infection by through-route from Egypt, they remained sterile.

Southampton 17 Sept. 1865.

Southampton.—The first death from cholera, in Southampton, took place on the 24th September 1865, the case dating from the 17th of the month. There were altogether between the latter date and the 4th November, in Southampton and the vicinity, 60 cases of cholera (27 men and 33 women) of which 35 died.

Cases of cholera ending fatally occurred on two of the Peninsular and Oriental Company's vessels, the "Ellora" and "Nyanza," in their homeward voyage from Alexandria in the month of July, cholera being prevalent in that city at the time of their departure. The "Ellora" reached Southampton on the 10th July, and ran into port with diarrhœa among the crew and passengers. The "Nyanza" arrived on the 22nd July, having lost a passenger from cholera five days before her arrival.

* Rapport sur la Marche, &c., p. 25.

† See concerning the cases in Altenburg, Dr. Rudolf Gunther's work, "*Die indische Cholera in Sachsen im Jahre*, 1865," (Leipzig), pp. 9–11.

The officers and crew of this ship had suffered more or less from diarrhœa.

Diarrhœa broke out among the crew of another of the Peninsular and Oriental Company's ships, the "Delta," while lying at Alexandria in August. The day the "Delta" sailed on her homeward voyage, the 28th August, a passenger was received on board suffering from diarrhœa, and he remained on the sick-list until the 10th September, the day before the vessel reached Southampton. Some of the crew were so ill from diarrhœa towards the termination of the voyage as to be off duty from the 7th September to the 10th.

These facts must not be taken as representing the whole amount of diarrhœal affection, among the passengers and crews of the Peninsular and Oriental Company's ships, running between Alexandria and Southampton, from the time of the appearance of cholera in the former place to the appearance of the disease in the latter. They simply represent the facts recovered on this subject some time after the manifestation of cholera in Southampton, when it was impossible to obtain the history of every ship with such precision as was desirable. The facts, indeed, indicate what may have happened in a greater or less degree in every ship that came into Southampton from Alexandria at this period, for so imperfect were the means of eliciting information at the time of the arrival of vessels, that the "Ellora" ran into Southampton with cases of diarrhœa on board, and after having lost cases from cholera, without the facts becoming known, even to the quarantine officers, until months afterwards.

Professor Parkes, F.R.S., made the outbreak at Southampton a subject of elaborate inquiry, under instructions from the Privy Council. He ascertained that the persons earliest attacked were, from the nature of their occupation, more exposed to chances of contagion introduced into the town and vicinity from the port than the rest of the community, although none had had communication direct or indirect with the Peninsular and Oriental Company's vessels.*

Theydon Bois, Essex (a parish in the Ongar hundred, containing, in 1861, 165 inhabited houses, and a population of 610 souls).—There occurred here, in an isolated farmhouse, and in direct or indirect connection therewith, at the close of September and beginning of October 1865, 12 cases of cholera, of which nine died. On the 25th September the head of the house and his wife returned home from Weymouth, where they had been staying several days, one or both suffering from diarrhœa. They had travelled to London by express train, passing through Southampton West on the journey, but not stopping there, so far as could be ascertained, except during the ordinary halt of the train at the station.† From the 28th September to the 6th October, inclusive, eight members of the family, including the head of the house, his wife, a maid-servant, and servant boy, were attacked with cholera. Of these persons five died, one, a child aged eight years, after less than 12 hours illness, and three during the stage of

Theydon Bois, 28 Sept. 1865.

* See *Eighth Report of the Medical Officer of the Privy Council*:—"On the Outbreak of Cholera in and about Southampton in September and October 1865," p. 392.

† This statement must be taken with some qualification. Both the farmer and his wife, who alone could have given precise information on the subject, were dead when I investigated this outbreak for the Privy Council. I have since had reason to believe that the wife may have visited one of the waterclosets at the station during the halt of the train, assuming no longer delay there. (See on this outbreak the "*Eighth Report of the Medical Officer of the Privy Council*;" also, "*Transactions of the Epidemiol gieal Society of London*," vol. 3, p. 85.)

consecutive fever. Within the same period the family medical attendant and a labourer employed about the house were both seized and both died, the former after 10 hours' illness. On the 10th October a woman who had assisted in laying out the corpse of the labourer was attacked and died the next day. Finally, a grandchild of this woman was seized with choleraic symptoms on the 31st October, and died in 36 hours.

All the cases but three (those of the medical attendant, the woman last mentioned, and her grandchild,) appeared to have been determined by the use of water from a well polluted by leakage from a sink-drain and from the soil-pipe of a watercloset into which had been cast, first, the diarrhœal discharges of the head of the house and his wife, and subsequently the "rice-water" evacuations of the first two patients seized with cholera.

General considerations from the different appearances of cholera described.

The different appearances of cholera which I have thus attempted to describe were the beginnings of the epidemic in Europe. I have dealt with them separately because they enable us to study with much clearness the manner of progress of the disease, and give the clue to its dissemination when it enters upon the great thoroughfares of the Continent, and within the active life and rapidly interchanging movements of the different populations, when it becomes impossible to follow the diffusion in detail. It is to be observed—

1. That the epidemic invaded Europe at spots, and at such spots only, as were in the most frequent and directest communication with Alexandria.
2. That in no instance did the invasion of the disease occur before there had been abundant opportunity for infection of the population invaded, assuming the disease to be infectious.
3. That in several instances, *e.g.*, at Constantinople, Pistoia, Valencia, Altenburg, the introduction of the disease and subsequent spread in direct relation to the case or cases introduced was obvious.
4. That in other places, *e.g.*, Marseille, Borchi, Malta, Ancona, Southampton, the inference of introduction of the disease, as the starting point of prevalence, is, from the preceding and concurring events, as certain as if the different steps had been as clearly observed as in the places previously mentioned.
5. That these conclusions apply equally to the places secondarily invaded, as Kustendji, the Danubian ports, and Odessa from Constantinople; Gibraltar from Malta; and Theydon Bois from Southampton.
6. That the facts recorded of Marseille and of Malta would appear to indicate that there is a period of the disease, as it is about to become prevalent or is becoming prevalent in a locality, when it is peculiarly transmissible, or is liable to be transmitted unrecognised. The transmission to Malta and Marseille took place almost certainly before the existence of cholera in Alexandria had become officially recognized. Some of the apparent mystery of the mode of transmission in these instances no doubt depends upon imperfect observation. But the transmission to Southampton, and through Southampton to Theydon Bois, shows how much we have yet to learn of the obscurer modes of transmission of the disease, or in other words, of its slighter, perhaps unrecognized, and not fatal forms. The introduction to Borchi forms in some sort a parallel to that of Theydon Bois, the introducers in both cases having passed rapidly through a district in which cholera was about to become

prevalent. Other instances of the same class are recorded in this report.

7. The conclusions here arrived at or suggested from the phenomena of the invasion of Europe are the same as those derived from the phenomena of the invasion of Egypt. Similar conclusions follow from the invasions I have still to describe, each separate invasion adding to the force of the conclusions derived from other invasions.

I now proceed to a description of the progress of the epidemic on the Continent in 1865 and the four subsequent years. Here I make no pretension to completeness, and the details I have to give must be regarded simply as materials towards the compilation of a complete history.

§

Diffusion in Europe, 1865.

1865.—From and through the several points of invasion which have been described, cholera penetrated into and became diffused in several parts of Eastern, Southern, and Central Europe, and into one part of Western Europe in 1865. It spread into southern, central, and northern Turkey in Europe, and along the valley of the Danube as high as the Hungarian frontier. It extended up the valley of the Sereth and the Pruth, and became widely diffused there, and in other districts of Wallachia and Moldavia. Contemporaneously with this diffusion it spread over Bessarabia and South Russia from the Wallachian border to the Don, sending hence, as already stated, a forerunner into Central Europe, at Altenburg, in Saxony.

While this diffusion was in progress in Eastern Europe and had begun in Central Europe, in Southern Europe cholera, beginning first at Ancona, had spread over the Adriatic provinces of Italy, and extended into several of its northern and western provinces. In Western Europe, moreover, the disease had become widely diffused in France, attacking especially the Mediterranean Departments of Bôuches-du-Rhone, Herault, and Var, and the metropolitan department of the Seine. In Spain also the Mediterranean provinces (including the insular dependency of Majorca) were especially affected, the disease also spreading into several of the southern and central provinces. In England there was no further diffusion than that already noted at Southampton and Theydon Bois. (*See* Map II.)

Of the diffusion on the Continent which I have thus summarily described the following are the most important details in my possession.

Turkey in Europe.

Turkey in Europe.—Very little is known of the diffusion of cholera in Turkey in Europe during 1865, beyond the scattering of the disease along the coast of this part of the Empire. South of Constantinople, Enos, the districts adjoining Cavalla, Salonica, Volo, and Larissa were affected; north of Constantinople, Kustendji; and on the Danube, Rustchuk, Tultcha, and Widin. In the interior, Phillipopolis, Pasardjik, Seres, and Filurina are reported to have suffered. With the exception of Constantinople, and the different quarantine stations of the Empire, the details of the movements of cholera in the various localities infected are very meagre. In Constantinople, from the 28th June to the close of September, the disease caused from 12,000 to 15,000 deaths in a population estimated at 900,000. At Therapeia, on the Bosphorus, there were from 130 to 140 deaths. At Enos, there were 56 cases of cholera, of which 52 died, in a population of 2,500,

from the 17th August to the 25th September. At Salonika, only three deaths from cholera were reported, but "many villages" were infected lying between Salonika and Cavalla on the coast, and Seres in the interior. The villages first infected near Salonika were those through which persons in quarantine were taken to the lazaretto, and where they halted. From these villages, some of which, and especially Galatzita, suffered very severely, the disease spread into the interior. In Volo, one case of cholera is stated to have happened, but 32 deaths from the disease were reported from neighbouring villages. In Larissa, there were 18 cases, and seven deaths reported from 5th to the 15th December inclusive. At Kustendji, cholera caused 120 deaths in August and September, 11 among the English residents. On the Danube, in the Bulgarian towns, the disease appears to have been more fatal. In Rustchuk, 360 cases and 131 deaths were reported in the 16 days following the 23rd August, among a population of 22,000; in Tultcha, 200 deaths from the 4th August to the 16th September, among a population of 20,000; at Widin, 300 cases and 110 deaths among a population of 25,000. Of the losses occasioned by cholera in the interior nothing has been made known, except with regard to Filurina, where from the 27th October to the 8th November there were 61 cases and 19 deaths, among a population of 7,000.

How far these meagre and imperfect data indicate the extent of prevalence of cholera in Turkey in Europe I am unable to state. At the time of prevalence of the disease, Her Majesty's representatives in the northern districts believed, that it was as prevalent on the Bulgarian as on the Rumanian side of the Danube. If this were the case, the facts stated, as will subsequently be seen, help very little to a just estimate of the extent to which cholera prevailed in Bulgaria.

Although the data relating to the diffusion of the disease on the mainland are very imperfect, those referring to its occurrence in the different quarantine stations in the empire are fairly complete, and are of much interest. I have summarised the more important of these in the accompanying Table, including the stations of Turkey in Asia with those of Turkey in Europe (see p. 59).

Rumania, 1865.

Rumania.—According to official reports, cholera appeared in this State, in 1865, on the Danube, first at Brahilov, on the $\frac{19\text{th}}{31\text{st}}$ July, and next, at Galatz, on the $\frac{24\text{th July}}{5\text{th August.}}$ It extended to the 33 towns and districts, and in several of these (Bukharest, Bottishani, and Jassy) it was still prevalent at the close of the year. The dates of appearance of the disease in the more important places attacked after Brahilov and Galatz were as follows:—Reni, $\frac{29\text{th July}}{10\text{th August}}$; Ismail, $\frac{1\text{st}}{13\text{th}}$ August; Bolgrad, $\frac{2\text{nd}}{14\text{th}}$ August; Bakeu, district, $\frac{18\text{th}}{30\text{th}}$ August, town, $\frac{24\text{th August}}{5\text{th September}}$; Byrlat, $\frac{27\text{th August}}{8\text{th September}}$; Bukharest, $\frac{5\text{th}}{17\text{th}}$ October; Jassy, $\frac{10\text{th}}{22\text{nd}}$ November. The greater number of the places to which the disease extended were in Moldavia and in Eastern Wallachia. Within the period named ($\frac{19\text{th}}{31\text{st}}$ July to $\frac{31\text{st December 1865}}{12\text{th January 1866}}$) 9,917 [? 10,057] seizures and 4,782 [? 3,930] deaths from cholera were registered. (See *Appendix*, Table II.)

Russia in Europe, 1865

Russia in Europe.—Very little was known of the different epidemics of cholera from which Russia has suffered, until the publication, last year (1874), of a treatise on the subject by Dr. Arkhangelsky, of

Table showing the Occurrences of Cholera in the principal Quarantine Stations of Turkey, 1865.*

Quarantine Station.	No. of Ships in Quarantine.	No. of Crews.	No. of Persons detained in Lazaretto.	Duration of Quarantine.	Greatest No. under detention at one time.	Cases of Cholera occurring on Ships in Quarantine.	Cases of Cholera occurring in the Lazaretto.	Deaths from Cholera in the Lazaretto.	Nature and Position of Lazaretto.	Cholera in Town or District adjacent to Lazaretto, and Remarks.
Sulina	887	7,983	518	5–10 days	73	30	12	5	Two buildings, containing together 8 rooms, and some huts outside the town.	Upwards of 300 deaths in the town.
Kustendji	95	928	580	3 days	—	11	—	—	Tents two miles from town.	140 cases in town, including several persons of quarantine service.
Bourgas	186	1,718	1,096	3 days	—	3	—	—	Huts	Two quarantine guards.
Enos	75	579	63	—	—	—	—	—	- - - - - - -	15 deaths in the town.
Cavalla	28	635	396	—	—	5	Many cases cholerine.	—	"Un vaste local" one hour from town; hospital on an islet.	Town exempt.
Salonika	78	—	4,257	5–20 days	1,300	—	265	122	1, One hour distant from town. 2, Temporary huts 3 hours distant.	Town 3 cases. Propagated to villages traversed by the detained in going to the lazaretto, and where they halted; and thence to neighbourhood of Seres.
Volo	25	526	2,265	—	—	5	57	23	Tents on island in gulf	1 case from infected village in interior. 9 cases, 4 deaths, lazaret service.
Mytilene	305	1,420	2,655	—	—	—	2	—	- - - - - - -	Island exempt.
Rhodes	288	2,501	2,618	10 days	—	—	1	1	Partly temporary encampment of tents.	Do.
Crete	103	843	972	10 days	—	11	13	9	Temporary encampments on islands in gulf of Sudha.	Island exempt. One fatal case among lazaret service.
Valona	22	—	416	10 days	—	5	—	2	Island, tents.	Town free.
Gallipoli	80	472	109	—	—	—	—	—	- - - - - - -	—
Dardanelles	145	3,058	2,269	5–10 days	900	16	6	15	Permanent, adjacent to town.	339 deaths in the town. Earliest cases persons belonging to quarantine service or in communication with lazaretto.
Smyrna	—	—	1,701	—	—	14	4	10	- - - - - - -	Upwards of 2,000 deaths in the town.
Cyprus (Larnaca).	42	573	1,199	—	—	4	22	7	Permanent stone building adjoining town.	363 deaths in town.
Mersina	97	1,953	450	—	—	—	—	—	Well isolated although wretched	Severe outbreak. First case from Adana where disease prevalent.
Beyrout	50	950	3,600	—	—	18 (in passage from Alexandria).	30	15	Lazaretto supplemented by houses, and a hotel. No proper séparation of sick and healthy.	1,500 cases, 493 deaths in town.
Samsoun	56	1,960	3,170	5–10 days	307	18	6	12 (24 bodies landed from ships).	Commodious barracks with hospital, at a distance from town.	—
Trebizond	68	2,558	5,073	—	600	1 (several fatal during voyage).	—	39	Partly under tents	45 cases, 28 deaths in town.

* From data given in the Proceedings of the International Sanitary Conference, 1866 (*Rapport sur la Marche*, &c.).

St. Petersburg, to which reference has already been made (p. 52 *footnote*). This very important work, based upon official information in the possession of the Medical Department of the Russian Government, supplies a great want in epidemiological literature, and from it I shall take the data necessary to show the progress of cholera in Russia during the periods I shall have to consider.

The first appearance of cholera in South Russia, at Borchi, in the government Podolia, on the $\frac{26\text{th July}}{7\text{th August}}$ 1865, I have already described. Its next appearance was in the government of Kherson, at Odessa, on the $\frac{29\text{th July}}{10\text{th August}}$, and, according to Dr. Arkhangelsky, at Nicolaiev the same day. The disease then spread into neighbouring governments, appearing in Volhynia, August $\frac{11\text{th}}{23\text{rd}}$; Kertch-Yenikale (Taurida), August $\frac{17\text{th}}{29\text{th}}$; Kiev, $\frac{\text{September 25th}}{\text{October 7th}}$; Bessarabia, October $\frac{1\text{st}}{13\text{th}}$; Ekaterinoslav-with-Taganrog, October $\frac{16\text{th}}{28\text{th}}$; the Don, $\frac{\text{October 24th}}{\text{November 5th}}$; Voronej, November $\frac{13\text{th}}{25\text{th}}$; and Kharkov, November $\frac{15\text{th}}{27\text{th}}$. With the exception seemingly of Kertch-Yenikale, from which there is no record after $\frac{27\text{th October}}{8\text{th November}}$ and of Bessarabia and Voronej, where the disease intermitted in December, the epidemic continued into the next year, terminating for the time being in the goverments of the Don, of Podolia, and of Kherson (with Odessa), in January 1866; in the governments of Ekaterinoslav-with-Taganrog and of Kiev, in February; and of Kursk, and Kharkov, in April. During this first period of the epidemic, and its diffusion in eleven governments of South Russia, 13,315 persons were attacked, of whom 4,177 died. (See *Appendix*, Table VI.)

Italy, 1865.

Italy.—Beginning in the province of Ancona on the 7th July (See p. 49), cholera in 1865 extended to 34 of the 65 provinces into which Italy was then divided, and in these provinces it appeared in 349 townships and communes. It extended also to parts of the Papal Territory. The provinces chiefly affected were: Ancona, Capitanata, Napoli, Terra di Bari, and Terra d'Otranto (See *Appendix*, Table XX.). The following is a summary statement of the sickness and mortality caused by this diffusion furnished to the Registrar-General,* by Dr. P. Maestri, of the Italian Ministry of Agriculture, Industry, and Commerce:—

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* *Weekly Returns of Registrar-General*, 1866, p. 883:—Dr. Maestri precedes this table, and other statistical tables relating to the epidemic, given in the volume of Weekly Returns referred to, by a statement (the statement of the official report referred to below) that the epidemic began on the 25th June 1865, in the Province of Turin. This statement refers to a fatal case of cholera ("colera spontaneo, isolato") which occurred in Turin on that date. Another fatal case occured in the same city on the 7th July. These cases were considered at the time as instances of *cholera nostras*, and it was not until the 14th August that the first case of malignant cholera (an importation from Marseille) was observed. The number of deaths registered from cholera in Turin during the seven months, June–December 1865, was as follows:—June, 1; July, 1; August, 3; September, 0; October, 1; November, 9; December, 71. Total 86. (*Istoria Documentata delle Epidemie di Colera di Torino*, 1865 *e* 1866. *del Prof. Giuseppe Teresio Rizzetti.* The details relating to the prevalence of cholera in Italy in 1865, 1866, and 1867, I have chiefly taken from the two official statistical reports on the subject (*Statistica de Reyno d'Italia. Sanità Publica. Il Colera Morbus nel* 1865., Firenze, 1867; and, with the same prefix, "*Il Colera Morbus nel* 1866 *e* 1867," Firenze, 1870). In the first of these reports the outbreak commencing in 1865 is described as ending on the 10th March 1866. In the second report the prevalence of 1866 is described as beginning on the 12th January. In reality the epidemic in the kingdom was continuous from its beginning in 1865 to its end in 1867.

Italy, 1865.

Sex.	Population of Communes attacked.	Attacks.		Deaths.		
		Total.	Per 10,000 Inhabitants.	Total.	Per 10,000 Inhabitants.	Per 100 Attacks.
Males - -	1,867,419	12,143	65·0	6,707	36·3	55·7
Females - -	1,810,528	11,434	63·1	6,134	33·9	53·6
Total - -	3,677,947	23,577	64·1	12,901.	35·1	54·7
	[?3,823,751]*			[?12,887]*		

Austria.—The epidemic was first observed in this empire at Prosecco, a village near Trieste, on the 29th September 1865. Shortly afterwards (prior to the 5th October) nine cases, of which six were fatal, occurred in the city and suburbs of Trieste. Altogether 83 cases and 60 deaths were recorded in that port before the close of the year. The disease does not appear to have spread beyond Trieste and the immediate vicinity. *Austria*, 1865.

France.—Following upon the appearance of the disease in Marseille, in June 1865, cholera in the course of the next six months invaded 36 of the 85 departments of France. Paris was attacked, first in the suburban village of Puteaux, on the 18th September, and at the close of the year the epidemic had caused 6,441 deaths. In the greater number of the departments affected only scattered cases occurred, the stress of the epidemic falling upon Bouches-du-Rhône, Var, Herault, and Seine. The distribution of the disease in France, and approximative mortality from it,† are shown in the accompanying summary of a return published under the authority of the Minister for Agriculture, Commerce, and Public Works :—

Department.	No. of Communes attacked.	No. of Deaths from Cholera declared.	Date of Invasion of the Epidemic.
Bouches du Rhône -	17	2,196	17th July.
Vaucluse - -	22	71	5th August.
Var - - -	15	1,691	26th ,,
Herault - -	35	407	31st ,,
Savoie - -	1	3	6th September.
Pyrénées-Orientales -	1	32	,, ,,
Rhône - -	1	10	11th ,,
Seine - - -	Paris and rural communes.	6,383	22nd ,,
Yonne - -	1	1	1st October.
Vienne (Haute) -	1	5	,, ,,
Somme - -	4	16	1st ,,
Oise - - -	6	36	5th ,,
Nord - - -	2	33	6th ,,
Moselle - -	2	15	,, ,,
Eure-et-Loir - -	2	2	8th ,,
Seine-et-Marne -	10	44	9th ,,
Ariége - -	1	6	10th ,,
Allier - -	1	5	12th ,,

* The totals of several of the official returns given in the Appendix do not always represent accurately the sum of the columns of figures to which they are attached. Where necessary, I shall add the corrected total, with a mark of interrogation, in brackets.

† The return is given in detail in M. Jules Girette's interesting work, *La Civilization et le Choléra* ; Paris, 1867, p. 291.

Department.	No. of Communes attacked.	No. of Deaths from Cholera declared.	Date of Invasion of the Epidemic.
Finistère - -	9	95	15th October.
Pas-de-Calais - -	1	4	12th ,,
Seine-et-Oise -	26	220	14th ,,
Saône-et-Loire -	2	5	14th ,,
Deux-Sevres - -	1	5	15th ,,
Seine-Inférieure -	4	37	18th ,,
Gard - - -	1	6	29th ,,
Meurthe - -	3	4	3rd November.
Loire-et-Cher -	2	10	4th ,,
Vosges - -	2	44	28th ,,
Nièvre - -	1	4	25th ,,
Orne - - -	1	10	30th ,,
Calvados - -	1	38	1st December.
Loiret - -	1	3	5th ,,
Ille-et-Vilaine -	1	2	8th ,,
Manche - -	6	132	13th ,,
Morbihan - -	1	6	17th ,,
Loire Inférieure -	1	3	26th ,,
Total - -		10,584	

Spain, 1865.

Spain.—No official account appears to have been published of the progress of the epidemic in Spain. The following information relating to the disease there is obtained partly from the account prepared by Dr. Webster, F.R.S., from the Spanish medical journals at the time, and given in my first report, and partly from the facts communicated to the International Sanitary Conference of 1866, by the Spanish delegates.

From the commencement of the epidemic in Valencia the 8th July (*See* p. 39) to the 10th November, the disease had prevailed in 486 localities (towns, villages, and their vicinity), distributed in 22 provinces. In the province of Albacete, 23 localities; Alicante, 27; Badajoz, 91; Balearic Islands, 10; Barcelona, 7; Cadiz, 1; Castellan, 37; Ciudad Real, 5; Girona, 2; Guadalajara, 9; Huelva, 1; Jaen, 2; Madrid, 26; Murcia, 21; Segovia, 8; Sevilla, 20; Tarragona, 15; Teruel, 34; Toledo, 4; Valencia, 197; Valladolid, 1; and Zaragoza, 27. Subsequently 9 other provinces appear to have suffered from the disease, making a total of 31 invaded by the epidemic, out of the 49 into which the kingdom is divided.

In the town of Valencia, it is estimated, that from the date of introduction of the disease to the 22nd October, when it ceased, 5,100 deaths occurred among a population numbering, at the commencement of the epidemic, 107,000, but reduced by flight, during its progress, to 67,000. In the town of Carthagena (population 25,000) the deaths were 900; in the town of Murcia (population 37,000) 879. In both these towns the population was reduced probably one half, during the course of the epidemic, by the flight of the inhabitants. Cholera appeared in Seville on the 6th September, and prevailed there until the 30th November. Within that period there were 4,330 cases and 2,674 deaths, among a population estimated at from 130,000 to 140,000, but reduced 25,000, also from the flight of inhabitants, when the epidemic appeared. Barcelona (population 190,298) was attacked on the 22nd July, and 1,799 deaths from cholera were recorded from that date to the 15th November, when the disease ceased. It is stated that no less than half the population fled from the town at the commencement of the epidemic. In Madrid (population, in 1864, 475,785), from the earliest observed case on the 15th August to the 20th November, there were 2,869 deaths.

In Alicante (population, 21,000), the mortality was 517. Palma suffered a mortality of 2,892, among a population estimated at 50,000, but diminished one fifth by flight. These disconnected facts will indicate in some measure the extent of prevalence and the degree of severity of the epidemic in Spain.

Portugal.—This kingdom suffered only from a slight scattering of cholera across the Spanish frontier. The disease appeared at Elvas (Alantajo) on the 1st October, and caused there about 50 deaths. An infected person, going from Elvas to Oporto, sickened in the last-named town and infected three other individuals in the same house. Another outbreak occurred at Freixo d' Espada a Cinta (Tras-os-Montes), but it is stated to have caused only a few deaths. There do not appear to have been any other occurrences of cholera in Portugal in 1865.

Portugal, 1865.

Central Europe—Saxony.—After the appearance of cholera at Altenburg, Saxe-Altenburg, on the 27th August 1865, as already related (*See* p. 54), the disease extended to neighbouring districts of Saxony, and from that date to the 29th December it caused 468 deaths. Twenty-five localities were affected, but in 15 of these one death only occurred from cholera in each locality; in two, 2 deaths in each; and in two also (Crossen and Marienthal) 5 deaths in each.* The loss of life from the disease and its duration in the remaining localities are shown in the following table:—

Saxony, 1865.

Place.	Population, 1864.	Duration of Epidemic.	Deaths from cholera.
Altenburg - -	17,966	27th Aug.–15th Dec. - -	92
Werdau - -	10,548	30th Sept.–11th Dec. - -	261
Rasephas - -	246	14th Sept.–14th Oct. - -	12
Zwickau - -	22,432	15th Nov.–12th Dec. - -	14
Glauchau - -	19,296	28th Nov.–25th Dec. - -	32
Elsterberg - -	3,557	26th Nov.–14th Dec. - -	28

The British Islands.—The appearance of the epidemic in the British Islands was limited in 1865 to the outbreaks at Southampton and its vicinity, and Theydon Bois, which have been already described (*See* pp. 54–56).

The British Islands, 1865.

1866.—At the close of 1865 cholera had become quiescent in the greater number of places in which it had appeared in Europe, but in a few it still remained more or less active, as in certain districts of South Russia; and this activity was continued into the next year. As 1866 advanced, the epidemic reappeared in many districts and invaded others, and before the close of the year it had extended over the greater portion of Central and Northern Europe. In Turkey cholera reappeared at Constantinople and caused a few deaths there late in the year. It attacked Salonika, which town had escaped the previous year, again showed itself in several districts of Bulgaria along the Danube, and then, passing westwards, entered Bosna-Serai. In Rumania the disease became prevalent in the majority of the localities which had suffered from it in 1865, and it extended to others. The total number of localities affected by the epidemic in this country in 1866 numbered less than in

Diffusion in Europe, 1866.

* *Die indische Cholera in Sachsen*, 1865. Dr. Rudolf Günther, Leipzig, pp. 84, 85.

1865, but the sickness and mortality from it were very considerably greater. In Russia the disease spread over the whole country, with the exception of Finland and the province of Archangel. In Italy cholera was more widely diffused than in 1865. In Austria and Hungary the epidemic became general. In France it was probably as widely disseminated as in 1865. In that year 36 departments had been affected by it; in 1866 the unofficial and incomplete records which exist on the subject show that 35 were affected. Of these 35 departments, 15 were newly invaded in the course of the year. In Saxony the epidemic extended throughout the kingdom. In the British Islands it was widely diffused. Of Spain I have no information.

Such briefly was the course and general distribution of the epidemic this year in the countries of the Continent which had been invaded in 1865. In addition, the epidemic spread in 1866 over Belgium and the Netherlands, Prussia, Poland, and Sweden, attacked Norway slightly at a few points, and touched, still more slightly, Denmark. (*See* Map III.).

The loss of life from this year's diffusion in Europe, as the account of its distribution, is only imperfectly known. The following is a summary of the mortality in those countries of which some definite information on the subject has come to my knowledge. Other information on the same subject, relating to particular localities, is given in the subsequent accounts of the diffusion in the different countries which have been referred to:—

Country.	Population.	Deaths from cholera.
Rumania	3,864,848 (1860)	26,179
Russia in Europe	59,330,752 (1858)	72,586
Poland	4,840,466 (1860)	17,799
Austria (part of)	3,642,311*	96,879
Prussia	19,304,843 (1864)	114,683
Italy	21,776,953 (1862)	19,571
Belgium	4,940,570 (1864)	32,812
Netherlands	3,735,682 (1865)	19,686
Saxony	2,343,994 (1864)	6,736
Sweden	4,114,141 (1865)	4,503
Norway	1,701,478 (1866)	51
Great Britain and Ireland	27,927,485 (1861)	17,149
		428,634

* So stated in the official return of cholera used in this Report.

Turkey in Europe, 1866

Turkey in Europe.—Turkey appears to have suffered little from cholera in 1866. It reappeared in July at Tultcha and Rustchuk, on the Danube. At the latter town the disease was chiefly prevalent among troops encamped in the vicinity. Many of the villages in the district surrounding Rustchuk were attacked. Later in the year the disease appears to have been prevalent to some extent at Shumla, and in the neighbourhood of that town and military station. Subsequently it was reported to be prevalent in Belgrade, but nothing definite has been made known of the extent of its prevalence there and in Servia generally. In September cholera appeared in Bosna-Serai (Seraijevo), and spread to an unknown extent in Bosnia. Maglai and Sienitza were infected, and in Seraijevo there were 600 deaths reported from the 12th September to the 31st October, the disease ceasing there at the latter date. In October cholera reappeared in the suburbs of Constantinople at the

village of Ortikaioi. Here from the 9th October to the 20th November 14 cases and 12 deaths from cholera occurred, and 40 cases of diarrhœa. In November several cases, none fatal, happened on board ships moored off Ortikaioi and Beshiktash; and nine cases and eight deaths were reported scattered over the northern portion of the city, north of the Golden Horn. In November, also, the disease broke out in Salonika, and from that date to the 8th December, 70 cases and 31 deaths occurred there.

Rumania.—Cholera, in 1866, prevailed in 45 localities in Rumania as compared with 33 in 1865. Twenty-two of the localities in which the disease became prevalent in 1866 were newly attacked that year, namely, the towns and districts of Dimbovitza, Nemtu, Roman, Suceva, Rymnik-Valtchei, and Vasluiu, the districts of Faltchei, Golia, Ismail, Tecuciu, Tutova, Arges, and Teleorman, and the town of Caracal. The 23 localities in which the disease had prevailed in 1865, and in which it reappeared in 1866, were the towns and districts of Bakeu, Braila, Jassy, Cahul and Rymnik-Saratu, the districts of Bolgrad, Botosani, Buseo, Covarluiu, Ilfov, Ismail, and Dolgiu, and the towns of Galatz, Ismail, Ploesci, Byrlat, and Giurgevo. The greater number of the localities affected in 1866, as in 1865, are situated in Moldavia, in the valleys of the Pruth and Seres rivers, and in Eastern Wallachia within the district bordering the Danube. In Western Wallachia the disease extended up the valley of the Aluta as high as Rymnik-Valtchei.

Rumania, 1866.

The prevalence of cholera in Rumania, in 1866, began in the district of Jassy on the $\frac{4th}{16th}$ May, and ended in the town of Caracal on the $\frac{10th}{22nd}$ October. Within this period there were 65,541 [? 64,853] seizures and 26,174 [? 29,020] deaths, the seizures in 1865 having numbered 9,917 [? 10,057] and the deaths 4,782 [? 3,930]. (See *Appendix*, Table III.).

Russia in Europe.—Cholera was still more or less prevalent in eight of the twelve governments of South Russia invaded by the disease in 1865, when that year came to a close.

Russia in Europe, 1866.

The following are the dates (New Style), of the cessation of the outbreak of 1865 in those provinces in which it continued until 1866, and of the reappearance of the disease in the same governments that year :—

Government.	Date of cessation of Outbreak of 1865. (New Style.)	Date of reappearance of Cholera in 1866. (New Style.)
Don Cossacks - -	20th January 1866 -	July 26th, 1866.
Podolia - - -	2nd February „ -	June 11th „
Kherson - - -	12th „ „ -	June 26th „
Ekaterinoslav-with-Taganrog	27th „ „ -	June 13th „
Kiev - - -	1st March „ -	March 27th „
Kharkov - - -	3rd „ „ -	July 5th „
Kursk - - -	11th „ „ -	June — „
Volhynia - - -	Continued into and through 1866.	——

The re-awakening activity of the epidemic in Russia was first observed, in March, in the government of Kiev, cholera having continued throughout the winter in the adjoining province of Volhynia. In the next month, April, the disease became again active in Bessarabia. This government, as that of Kiev, had suffered from the epidemic the

preceding year, but the disease had ceased there on the $\frac{5\text{th}}{17\text{th}}$ December In May the disease appeared beyond the area of the diffusion of 1865, in the government of Minsk, the first case being recorded there on the $\frac{6\text{th}}{18\text{th}}$ of the month. On the $\frac{30\text{th May}}{11\text{th June}}$ cholera reappeared in Podolia. About the same time the disease reappeared in the government of Ekaterinoslav-with-Taganrog, and extended into new ground in the government of Poltava. Next in order of succession of the epidemic's appearance came the government of Grodno, where the disease began on the $\frac{11\text{th}}{23\text{rd}}$ June.

The provinces here mentioned form a group which hem in Volhynia, and which have direct relations with that province or with each other. Volhynia, in fact, formed the centre of the early diffusion of cholera in this part of Europe in 1866. For in Galicia, in the Bukovina, the epidemic appeared at the beginning of May (on the 4th), here commencing its course in Austria; and in Moldavia it reappeared in the district of Jassy on the $\frac{4}{16}$th of the same month. Of the movement of the epidemic on the Polish frontier of Volhynia I have no information. Dr. Arkhangelsky does not include in his work the cholera statistics for 1866 in Poland, but from the severity of the epidemic in this division of the Russian Empire during that year, it may perhaps reasonably be inferred that the progress of the disease in the government of Lublin was no exception to that observed in other adjacent governments and countries.

On the $\frac{14\text{th}}{26\text{th}}$ June cholera appeared in St. Petersburg, and the same day it reappeared in the Governments of Kherson and the Don Cossacks. The next day, the $\frac{15\text{th}}{27\text{th}}$, the disease re-appeared in Taurida, and the day following, the $\frac{16\text{th}}{28\text{th}}$, it showed itself in another government previously free from the epidemic, Moscow. From the dates of invasion of the governments of St. Petersburg and Moscow the relation of the successive outbreaks to the original centre of diffusion in the south-western provinces is no longer apparent in the tabulated records. After the $\frac{16\text{th}}{28\text{th}}$ June the epidemic became manifest in the several governments still unaffected in the months following and in the order stated. In *July*, Tchernigov ($\frac{25\text{th June}}{7\text{th July}}$), Tver ($\frac{26\text{th June}}{8\text{th July}}$), Olonetz ($\frac{29\text{th June}}{11\text{th July}}$), Orel and Kursk (dates not given), Jaroslav ($\frac{1\text{st July}}{13\text{th July}}$), Esthonia ($\frac{3\text{rd}}{15\text{th}}$), Kasan ($\frac{3\text{rd}}{15\text{th}}$), Vologda ($\frac{5\text{th}}{17\text{th}}$), Livonia ($\frac{7\text{th}}{19\text{th}}$), Tambov, Kaluga, and Vilna ($\frac{8\text{th}}{20\text{th}}$), Pskov and Voronej ($\frac{13\text{th}}{25\text{th}}$), Vitebsk ($\frac{15\text{th}}{27\text{th}}$), Saratov ($\frac{16\text{th}}{28\text{th}}$), Tula ($\frac{19\text{th}}{31\text{st}}$). In *August*, Kovno ($\frac{21\text{st July}}{2\text{nd August}}$), Nijni-gorod ($\frac{22\text{nd July}}{3\text{rd August}}$), Courland ($\frac{23\text{rd July}}{4\text{th August}}$), Timbirsk ($\frac{24\text{th July}}{5\text{th August}}$), Mohilev (date not stated), Kostroma ($\frac{1\text{st}}{13\text{th}}$ August), Astrakhan ($\frac{3\text{rd}}{15\text{th}}$), Samara ($\frac{5\text{th}}{17\text{th}}$), Penza ($\frac{9\text{th}}{21\text{st}}$), Riazan ($\frac{10\text{th}}{22\text{nd}}$), Vladimir ($\frac{13\text{th}}{25\text{th}}$), Perm, ($\frac{14\text{th}}{26\text{th}}$), Viatka ($\frac{17\text{th}}{29\text{th}}$). In *September*, Smolensk ($\frac{27\text{th August}}{8\text{th September}}$), Orenburg ($\frac{3\text{rd}}{15\text{th}}$ September), Ufa* ($\frac{11\text{th}}{23\text{rd}}$).

The intensity of the epidemic varied very considerably in the different Governments. It was greatest in Bessarabia and Podolia; and next in order of intensity came St. Petersburg, Kherson, Grodno, Volhynia, Ekaterinoslav-with-Taganrog, Kursk, and Poltava.

The diffusion of this year, starting from Volhynia, where the disease had existed throughout the winter, appeared in one province in March,

* Ufa is a Government, with the town of Ufa as capital, constituted by a division of the former Government of Orenburg.

one also in April, and one in May; 10 provinces in June, 20 in July, 12 in August, and 3 in September. It had not entirely ceased when the year closed, and it continued in the province of Tambov until the $\frac{19th}{31st}$ January 1867, and in the province of Minsk until the $\frac{31st\ January}{12th\ February}$. From the $\frac{1st}{13th}$ January 1866 to the $\frac{31st\ January}{12th\ February}$ 1867, the number of attacks was 208,858 [? 207,953], and of deaths 72,386. (See *Appendix*, Table VII.).

Poland.—The returns for Poland are not included in Dr. Arkhangelsky's account of the prevalence of cholera in Russia in 1866. According to an official return furnished to this department, cholera, in that year, caused 43,007 seizures and 17,799 deaths in this kingdom. The details of distribution of the disease in the several governments of the kingdom are not given, but it would appear that the first case of cholera was observed in Warsaw on the $\frac{11th}{23rd}$ July. The fixed population of Poland in 1865 was 5,336,210, the floating 206,962, total 5,543,172. *Poland*, 1865.

Italy.—Throughout the winter of 1865–66 and following spring, cholera had not wholly ceased in Italy. In December 1865, 746 deaths from the disease had been recorded, and in the three succeeding months, January, February, and March, 1866, the numbers were respectively 39, 16, and 3.* In April 2 deaths were recorded, in May 1 only, and in June 3. The next month, July, the disease became active, 76 deaths being recorded during the month, and at the close of the year the mortality had reached 19,571. In the progress of this year's prevalence 45 provinces were affected as compared with 34 in the previous year. All the provinces which suffered from the disease in 1865, with three exceptions (Ascolo Piceno, Macerata, and Ravenna), were again affected, although in some instances but nominally, in 1866. One only of these provinces suffered to a greater extent in 1866 than in 1865, namely, Naples, the mortality in the first-named year (the year under consideration, 1866) having been 5,393; in the last-named year (1865), 3,379. On the other hand the mortality which in 1865, had been in Ancona, 3,138, Capitanata 2,336, and Terra di Bari 1,636, was, in 1866, in these provinces respectively only 7, 70, and 77. The provinces in which the epidemic prevailed most in 1866 were Palermo, Naples, Genoa, and Cuneo. (See *Appendix*, Table XX.). The following is a summary statement of the mortality from this year's diffusion in Italy:— *Italy*, 1866.

Italy, 1866.

Population of Communes attacked.	Deaths from Cholera.			
	Males.	Females.	Total.	Per 10,000 of population.
5,160,620	10,348	9,223	19,571	37·3

Notwithstanding the prevalence of cholera in 1865 and 1866 in numerous parts with which Sicily was in regular communication, that island escaped the disease until September of the latter year. This freedom from the epidemic was attributed to the great stringency of the quarantine maintained in its ports. In September 1866 an insurrection broke out in Palermo, and it became necessary to despatch a body of *Sicily*, 1866.

* So stated in the official Report for 1865 (p. 96); but in the the official Report for 1866–67, the deaths from cholera in these months are stated to have been, January 5, February 5, March 2.

troops there from Naples, where cholera was prevalent, for its suppression. These troops were landed at once on their arrival, the quarantine regulations being set aside under the emergency. On the 18th September a detachment arrived in the harbour of Palermo among whom several cases of cholera occurred the same day. The disease next appeared among the civil population of the portion of the town adjoining the parts first occupied by these troops, namely Castelluccio and Via dell' Acqua Santa. The civil lazaretto situated in the street just named, was converted for the time being into a cholera hospital, and when on the 22nd September communications had been re-established with the city, 22 cases of cholera, soldiers and civilians were under treatment there. The disease now spread into the city and prevailed in it until the 29th December, killing, from first to last, 3,977 persons, of whom 405 were soldiers.*

From Palermo the disease extended to neighbouring districts of the island, and from the date of its introduction to the end of the year caused not less than 7,273 deaths, of which number 5,688 occurred in the province of Palermo.

Austria, 1866.

Austria.—Cholera in 1865 had effected a lodgment at one spot, at least, in the Austrian Empire, namely, Trieste. Here 83 cases of the disease, of which 60 died, were recorded in that year. In 1866 cholera reappeared in that town and caused 432 deaths, the cases numbering 734. The disease, moreover, extended this year throughout the greater portion of the Empire. The special information in my possession regarding this diffusion does not include the district in which Trieste is situated (Istria), and the neighbouring districts of Carniola, Croatia, Slavonia, and Dalmatia. Hungary also is not included, although cholera is known to have been widely diffused in that division of the Empire in 1866. The following Table shows the extent of prevalence of the disease in other parts of the Empire.†

It will be observed that the starting point of the diffusion of 1866 in Austria, so far as the following data throws light upon it, was not in the southern district which had been infected the previous year, but in the Bukovina. This district is contiguous to the provinces of Russia where cholera had persisted throughout the winter of 1865–66, and where it had earliest manifested activity in the spring of 1866.

Austria, 1866.

Provinces.	Dates of beginning and cessation of Diffusion.	Number of Localities affected.	Population.	Cholera.	
				Attacks.	Deaths.
Bukovina -	20th May–30th Nov.	150	282,632	12,003	5,335
Bohemia -	10th June–30th Sept.	1,623	1,362,741	65,363	30,367
Galicia -	3rd July - -	(*see* 1867)	—	—	—
Moravia -	9th July–8th Sept. -	1,584	1,361,778	109,368	48,758
Styria - -	1st Aug.–17th Nov. -	47	24,501	453	293
Silesia -	11th Aug.–30th Sept.	160	204,234	5,838	2,217
Lower Austria	27th July–30th Sept.	498	406,545	26,527	9,909

* *Il Colera di Palermo nel* 1866. Relazione de Cordao Tommasi già Direttore del servizio Sanitoria Municipale.

† Dr. Arkhangelsky states that according to the Central Statistical Committee of the Austrian Empire, there were in Hungary, in 1866, 69,628 deaths from cholera, the total deaths from the disease in Austro-Hungary being 234,920.

France.—No official general return of the mortality from cholera, and of its distribution, in the different parts of France, in 1866 and subsequent years of the period considered in this report, has been published. Such knowledge as exists on the subject is chiefly contained in the information on epidemics in France communicated to the Academy of Medicine and reported upon annually. The report presented to the Academy for 1866 * shows that cholera had been present that year in 229 communes, scattered over 66 arrondissements, in 34 departments. But this return does not represent the whole extent of prevalence of the disease, for from many localities the Academy had not received information. Such as it is, when compared with the official return for 1865, it proves that the disease was more extensively diffused in France in 1866 than in the year previous. In 1865 the number of communes affected had been 186, scattered over 36 departments. The names of 17 departments appear in the report of the Academy that were newly infected in 1866; these were Aisne, Alpes-Maritimes, Ardennes, Aube, Charente-Inférieure, Cher, Côte-d'Or, Marne, Marne (Haute), Meurthe, Meuse, Morbihan, Puy-de-Dôme, Rhin (Bas), Sarthe, Sévres (Deux), and Vendée. Of the 36 departments infected in 1865, the same report shows that the disease reappeared in 18 in 1866, namely, Nord, Seine-et-Maine, Finistère, Pas-de-Calais, Seine-et-Oise, Seine-Inférieure, Gard, Meurthe, Loire-et-Cher, Nièvre, Calvados, Ille-et-Vilaine, Manche, Morbihan, Loire-Inférieure, Bouches-du-Rhône, Hérault, and Yonne.

The departments, and the number of arrondissements and communes in them, affected with cholera in 1866 according to the report of the Academy of Medicine, were as follows:—

Department.	Affected with Cholera.		Department.	Affected with Cholera.	
	Arrondissements.	Communes.		Arrondissements.	Communes.
Aisne - -	1	2	Marne - -	1	1
Alpes-Maritimes	1	8	Marne (Haute) -		
Ardennes -	2	2	Meurthe -	2	14
Aube - -	1	1	Meuse - -	3	8
Bouches-du-Rhône	1	2	Morbihan -	5	43
Charente-Inférieure.	2	18	Nièvre - -	4	13
			Pas-de-Calais -	1	3
Cher - -	1	1	Puy-de-Dôme -	2	4
Côte d'Or -	2	5	Rhin (Bas) -	—	Several.
Cotes-du-Nord -	3	18	Sarthe - -	1	1
Finistère -	2	17	Saône (Haute) -	1	1
Gard - -	1	1	Seine-Inférieure	1	1
Hérault - -	1	1	Seine-et-Marne -	4	17
Ille-et-Vilaine -	3	9	Seine-et-Oise -	4	5
Loir-et-Cher -	2	6	Sévres (Deux) -	1	5
Loire-Inférieure -	1	1	Vendée -	1	7
Maine-et-Loire -	1	1	Yonne - -	2	7
Manche - -	1	1			

The report of the Academy gives no account of cases and deaths in the several localities where cholera prevailed in France in 1866. It does not even refer to the prevalence of the disease in Paris and the Department of the Seine, the report being restricted to the information directly communicated to the Academy. Paris suffered from cholera to almost as great an extent in 1866 as it had suffered in 1865. The following

* Mémoires, t. 28.

return, in which I have also included the facts for 1865, is derived from the *Bulletin de Statistique Municipale*, published monthly under the authority of the Prefect of the Seine.

Deaths from Cholera and Diarrhœa in Paris, 1865-1866.

Months.	1865.		1866.	
	Diarrhœa.	Choleraic Diarrhœa and Cholera.	Diarrhœa.	Choleraic Diarrhœa and Cholera.
January	27	4	24	23
February	22	4	37	9
March	19	10	29	11
April	29	7	30	5
May	37	17	32	9
June	47	26	42	12
July	81	73	73	1,743
August	111	71	74	2,495
September	109	179	61	967
October	150	4,653	31	217
November	72	1,318	18	12
December	37	291	27	6
	741	6,653	478	5,509

Calvados is another department which was affected with cholera in 1866 not referred to in the report of the Academy of Medicine. From a report on the prevalence of cholera in this department in 1873, by Dr. Denis Dumont*, it incidentally appears that in 1866 the disease occurred in a small hamlet of the commune of Bretteville-au-Laize, in February of that year, and attacked there 30 persons, of whom 20 died. It caused also 25 deaths in the commune of Oyestreham, and 215 deaths in the town of Caen, the cases in the last-named place numbering 620.

Belgium, 1866.

Belgium.—Dr. Van den Corput states† that Belgium was invaded by cholera in 1866 at four points. The disease was imported from France into Roosbrugghe-Haringhe on the 15th March, and into Messancy (Luxemburg) on the 1st May; from Holland into Gand on the 11th May; and by a Bremen ship, carrying emigrants, into Antwerp on the 15th May. These were the starting points of the subsequent diffusion in the kingdom, of which the general results are given in the accompanying table, and which attacked 62,899 persons, and caused from the 1st May to the 15th October, inclusive, 32,812 deaths, among a population o 4,893,021.

* *Rapport sur l'Epidémie cholérique de* 1873 *dans le Calvados.*

† *Bulletin des Epidémies* (*Journal Publie pour la Société Royale des Sciences Médicale et Naturelle, Bruxelles,* 1866).

Belgium.*—(*1st May to 15th October* 1866.)

	Population, 31st December 1863.	Cholera.	
		Cases.	Deaths.
Provinces.			
Anvers	471,908	9,181	4,588
Brabant	839,301	15,533	9,034
Flanders, West	652,372	3,703	1,950
Flanders, East	816,232	9,216	5,114
Hainault	845,961	9,836	4,104
Liége	554,739	10,988	5,822
Limbourg	199,242	412	216
Luxembourg	206,291	1,975	974
Namur	306,975	2,055	1,010
Total	4,893,021	62,899	32,812
Towns.			
Anvers	120,444	4,865	2,306
Bruxelles	184,932	3,966	3,028
Bruges	50,981	1,511	773
Gand	122,900	4,135	2,187
Mons	27,173	772	403
Liége	101,710	4,330	2,582
Namur	26,204	1,019	492
Total	634,344	20,598	11,771

Netherlands.—No province of the Netherlands escaped the diffusion of 1866. The total mortality from cholera throughout the kingdom during the year was 19,686, the population being estimated on the 31st December 1865 at 3,530,047. The distribution of the mortality in the different provinces was as follows :—† *Netherlands*, 1866.

Province.	Population, 31st Dec. 1865.	Deaths from Cholera.	Date of first recognised Case.
Gelderland	427,852	1,458	20th April (Herwijnen).
South Holland	672,367	7,688	8th April (Rotterdam).
North Holland	566,803	2,594	12th May (Haarlemmerliede an Spaamwouda).
Zeeland	176,169	252	19th May (Tholau).
Utrecht	172,787	2,695	6th April (Utrecht).
Friesland	288,991	461	19th May (Lemsterland).
Overyssel	250,766	1,017	11th June (Genemuiden and Zwartsluis).
Groningen	224,237	1,525	13th May (Wildervank).
Drenthe	104,037	384	4th June (Hoogeveen).
North Brabant	396,420	1,167	23rd April ('sHertogenboosch).
Lemburg	222,578	450	1st July (Sint Pieter).
Netherlands	3,530,047	19,686	6th April (Utrecht).

Saxony.—In Saxony cholera reappeared in 1866 in the government of Leipzig, where the first death from the year's diffusion occurred on the 29th June; and the disease did not wholly cease until the 25th *Saxony*, 1866.

* Furnished by M. Heuschling, Secretary of the Central Statistical Commission of Belgium, to the Registrar-General (Weekly Returns, 1866, p. 885).

† *De Cholera epidemie in Nederland, in* 1866 *en* 1867.'s Gravenhage, 1873.

December, or thereabouts, when the last death was recorded in the government of Zwickau. In 1865 the disease had appeared in twenty-five places in Saxe-Altenburg and Saxony, and caused there 468 deaths. Seventeen of these places were in the kingdom of Saxony, and in these places 358 of the deaths occurred. In 1866 the number of places affected by the diffusion in the kingdom of Saxony was 330, and the mortality occasioned by it was 6,736. The distribution of this mortality in the several divisions of the kingdom, together with the period during which it occurred and the number of places affected by the disease, are shown in the following Table compiled from the official returns :—*

Governments.	Population, 1865.	Deaths from Cholera.	Number of Localities affected with Cholera.	Period during which the Deaths happened.
Dresden - -	615,169	236	27	4th July–22nd Oct.
Leipzig - -	532,689	3,376	133	29th June–26th Nov.
Zwickau - -	872,448	2,597	115	14th July–25th Dec.
Bautzen - -	316,886	527	55	21st July–30th Oct.
Total -	2,343,994	6,736	330	

Prussia, 1866.

Prussia.—Cholera appeared first, this year, in this kingdom, in the Government of Treves, Rhenish Prussia, on the 2nd February. The disease spread generally throughout the kingdom, with the exception of the province of Hohenzollern and the Territory of Jahde, prevailing in the Governments of Treves and Arnsberg until January 1867, in the government of Dusseldorf until February, and in the government of Merseburg until an unstated period in the same year. In the several Governments mentioned, and also in other parts of the kingdom, cholera reappeared in 1867. During the prevalence of cholera in Prussia, in 1866, the recorded attacks from the disease among the civil population were 224,382, and deaths 114,683.

The following is a summary statement of the distribution of the sickness and mortality in the several provinces of the kingdom, the distribution in the different Governments being given in the Appendix (See *Appendix*, Table XXVII.).†

Prussia.—Cholera 1866.

Province.	Civil population 1864.	Cholera. Attacks.	Cholera. Deaths.	Duration of diffusion.
Prussia - - -	2,982,215	36,600	19,161	6 June–21 Dec.
Posen - - -	1,505,944	42,023	20,161	15 „ –30 Nov.
Brandenburg -	2,476,148	32,137	17,949	2 „ –3 Dec.
Pomerania - -	1,418,721	20,716	14,102	29 May–30 Dec.
Silesia - - -	3,473,259	37,623	20,757	25 June–31 „
Saxony - - -	1,948,609	27,349	13,395	2 July–1867.
Westphalia -	1,374,697	5,074	2,435	28 June–14 Jan. 1867.
Rhine - - -	2,834,028	16,660	6,723	2 Feb. 1866–16 Feb. 1867.
Hohenzollern - Jahde - - -	Free from cholera.			
Totals - -	13,031,621	224,382	114,683	2 Feb. 1866–16 Feb. 1867.

* *Erster Jahresberricht des Landes Medecinal Collegiums, über das Medicinalwesen in Konigreich Sachsen* auf das Jahr 1867. Dresden, 1869.

† I am indebted for the particulars relating to the prevalence of cholera in Prussia in 1866 and 1867, to a paper by Dr. Engel, (Die Cholera-Epidemie des Jahres 1866 mit einen Rückblick auf die früheren Epidemien) published in the *Zeitschrift des Königlich Preussischen Statistischen Bureaus* for 1869, p. 70.

Denmark.—I quote Dr. Schleisner's account of the extent to which Denmark was affected by the diffusion of 1866 :—* *Denmark*, 1866.

"In 1866 when cholera prevailed in the greater number of the ports of the Baltic, 2,233 ships coming from ports or anchorages infected with the disease anchored in the roads of Copenhagen from the 6th May to the 7th November. Of these ships, 1,490 bound on long voyages anchored but a very short time in the outer roadstead ; 286 anchored for a longer time in the inner roadstead ; and 457 came into port for the purpose of loading or discharging cargo. Not less than 88 cases of cholera and suspicious diarrhœa were brought into the different anchorages, of which 30 were treated on board ships, whilst 58 were removed to a hospital specially established for the purpose at a distance from the city and quite isolated. In the city itself but four cases of cholera occurred. The first took place on the 8th October, the patient being the wife of a workman engaged in carrying coal, and who associated daily in the port with foreign sailors. Two days after two fresh cases of cholera occurred in the same house. The three patients were, as soon as their sickness was known, removed to the cholera hospital, and the inhabitants of the house who had communicated with them, eight in number, were also removed to an isolated locality, where they were kept under observation seven days. The fourth case took place eight days afterwards in another quarter of the city, and was dealt with in the same manner. I believe that the spread of the disease here was stopped by these measures."

Sweden.—The diffusion of 1866 extended to 25 of the 29 districts into which Sweden is divided, and in these districts it attacked 216 communes. The districts which principally suffered from the epidemic were Stockholm (town), Gotenburg, and Bohus, Elfsborg, Ostergötland, Wester-Norrland, Gefleborg, and Wermland. The attacks from cholera numbered 12,799, the deaths 4,503. The population of the infected districts in 1865 was 4,039,680, the total for the whole of Sweden being 4,116,141. The distribution of the attacks and deaths in the different districts of the kingdom is shown in the Appendix, Table XXI. *Sweden*, 1866.

Norway.—The incidence of the diffusion of 1866 upon Norway was very slight. The localities chiefly affected were the municipal districts of Christiana and Christiansand, 38 cases and 27 deaths occurring in the former district, and 15 cases and seven deaths in the latter district. The total number of cases in the kingdom was 79, and of deaths 51. These were distributed in the principal divisions as follows : Christiana (38 cases, 7 deaths) ; Akershus (2 cases, 2 deaths) ; Smaalene (1 case) ; Buskerud (12 cases, 7 deaths) ; Jarlsberg and Laurvig (9 cases, 7 deaths) ; Nedenœs (2 cases, 1 death) ; Manal (Christiansand, 15 cases, 7 deaths.) The several occurrences of cholera took place during the months of August and September, the first originating in the importation of the disease into Christiana.† *Norway*, 1866.

The British Islands.—The reappearance of cholera in England in 1866 was connected not with recrudescence of the disease in the localities which had been infected the previous year, namely, Southampton and Theydon-Bois, but with a series of re-infections from the Continent, one *The British Islands*, 1866.

* *L'apparition du choléra en Danemarc depuis sa première invasion en Europe, comparée avec l'apparition de la maladie dans les pays limitrophes et les ports voisins.* (Communicated to the International Sanitary Conference of 1874, and printed in the Proceedings of the Conference.)

† *Norges Officielle Statistik udgiven i aaret* 1868, *Medicinal Beretning* for 1866, p. xiv.

instance only excepted, where the source of re-infection was probably Egypt. The facts in reference to this subject, so far as they were then known, were given in my report on cholera in the metropolis in 1866, and I repeat them here with such additions as are necessary.*

"At the outset of the increased diffusiveness of the epidemic in 1866 England came within its range. Before, indeed, any news had reached this country of cholera having appeared in Holland, and before probably the existence of the disease was suspected in that country itself, two events had occurred at sea in ships sailing from an English port, of remarkable interest.†

"On the 28th March 1866 the screw-steamer 'England' sailed from the Mersey, [bound for New York,] having on board 807 passengers, more than half of whom were foreigners, Dutch and German, who, a few days before, had journeyed to Liverpool from Rotterdam by way of Hull. The vessel touched at Queenstown on the evening of the 29th, and there received additional passengers to the number of 393. Five days subsequently cholera appeared among the foreign emigrants, extended rapidly in the steerage, and when on the 20th April—17 days after the commencement—the outbreak came to an end, in Halifax harbour, the sick-roll included upwards of 500 cases, the death-roll at least 280.

"Six days after the 'England' had sailed from the Mersey, a sister ship, the 'Virginia,' followed from the same harbour. She had then on board 807 passengers, of whom 465 were foreigners who had also travelled to Liverpool from Rotterdam by way of Hull. This ship, as the 'England,' touched at Queenstown, to complete her complement. On the eighth day after sailing cholera broke out on board, again among the foreign passengers; and in 41 days, on the voyage and at the New York quarantine station, swept off 105 souls.

"Before a knowledge of these facts, and of the probable transmission of the infection of cholera across the kingdom, had reached England, an instance of importation of the disease into the West Midland counties occurred. On the 22nd of April, before which date cholera had shown itself in Rotterdam, a traveller sailed from that port for London. He had dwelt in the former city only since the 11th of the month, having on that day arrived there from Java. He reached the metropolis early on the morning of the 23rd, and proceeded at once by railway to Bristol. While in the train he was taken ill, and after 18 hours sickness he died, having manifested all the symptoms of confirmed Asiatic cholera.

"On the 2nd May two German emigrants died from cholera in Liverpool; others also succumbed to the disease in the town before embarkation and previous to the close of June. All had travelled to Liverpool by way of Rotterdam. During the two months three vessels carrying Dutch and German emigrants, sailed from the Mersey, each of which suffered from an outbreak of cholera. One, the 'Helvetia,' put back when the disease appeared, and her passengers underwent a sharp visitation in the Mersey.

"From the 13th May to the 26th of June five cases of cholera were registered in the borough of Liverpool, apparently 'quite unconnected with foreign emigrants.'‡ On the 1st July an undoubted case of

* On Cholera in London, and especially in the Eastern Districts (1866). *Ninth Report of the Medical Officer of the Privy Council*, p. 265.

† The earliest notifications I have seen of the presence of cholera in Europe in 1866, are Roosbrugghe-Haringhe, West Flanders, the 15th March; Utrecht, the 6th April; and Rotterdam the 8th April.

‡ See the Report of Dr. Trench, Medical Officer of Health for the Borough, on the health of Liverpool during the March and June quarters of 1866. Dr. Trench states that the "Virginia" left the Mersey "with 721 souls on board, of whom 260 were foreigners." The figures in the text were taken from official information

epidemic cholera among the ordinary population occurred, the starting point of the subsequent outbreak.

"But in the meanwhile the epidemic had appeared elsewhere in the kingdom. Between the 10th and 13th of June it broke out again in Southampton, and from the 12th to the 17th of the same month cases occurred at Northwich, in Cheshire, a small market town, situated about 24 miles in a direct line, S.E. of Liverpool and Birkenhead. On the 23rd June a boy died from cholera in the South Dock, Sunderland, on board a steamer from Stettin. On the 28th and 29th June two fatal cases occurred in Goole harbour on board an English steamer which had arrived the morning of the first-named day from Antwerp. On the 29th also a death from cholera took place on board a barque which had arrived that day, from Hamburg, in the Tyne, off Shields. A fatal case, moreover, occurred on the 1st July off the east coast at Harwich, in a vessel from Brussels; and another fatal case on the 3rd July on board a coasting vessel, off the south coast in Torbay."

The reappearance of the disease in Southampton was of peculiar interest. It followed upon the arrival in the port of the "Poonah," one of the ships of the Peninsular and Oriental Company, with cholera among the crew. She entered the port on the 10th June, a fireman having died on board the day previous from cholera; and several of the crew, who landed from her ill, were subsequently seen by medical men and were found to be suffering from severe choleraic diarrhœa. The disease spread in the town, and 101 cases, 48 of which were fatal, occurred during the eighteen weeks ending the 15th October. This outbreak was subjected to a detailed examination by Professor Parkes,† and the history, as then ascertained, appeared to show that the disease had originated among the crew after the ship had left Gibraltar, and that it had been determined by water, distinctly polluted by sewage, believed to have been taken on board there. There was a serious doubt, however, whether any water had been obtained for the ship at Gibraltar. The whole of the investigation by Professor Parkes was prosecuted under the belief, which at that time appeared to admit of no doubt, that cholera did not exist in Alexandria at the time when the "Poonah" sailed from that port, or at any of the intermediate ports touched at by the ship. I shall have to show when I describe the course of the epidemic in Lower Egypt, subsequent to 1865, that cholera had reappeared there early in 1866; and it is highly probable that the disease was present in Alexandria when the "Poonah" sailed from that port on the 28th May 1866, after 40 hours' stay there. No reappearance of the disease seems to have been observed in 1866, either in Malta or in Gibraltar, but in Lower Egypt there was a recurrence which persisted over several months, (Alexandria being affected among other places), and which was concurrent with reawakened activity of the epidemic in the Hejaz and on the coasts of the Red Sea (*See* pp. 95–99.) If the water which manifestly determined the outbreak on the "Poonah" was obtained from Alexandria, there can be little doubt of the source of its infection. If it were not obtained there, hardly less, doubt, I imagine, can exist that it, or the tank which contained it, in some way became infected there. But in whatever manner the question may be regarded of the mode of introduction of the infection on board the ship, and its relation to the water-supply contained in a particular tank, the cardinal fact is that the disease appeared when the vessel was thirteen days out from an infected district.

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furnished to the Department; but Dr. Trench's statement accords most with information subsequently obtained from the master of the vessel at New York (see p. 79).

† On cholera in Southampton (1866). *Ninth Report of the Medical Officer of the Privy Council*, p. 244.

App. No. 1.
On Cholera, by Mr. J. Netten Radcliffe.
Europe, 1866.

Cholera spread widely in England and Wales, less widely in Scotland and Ireland during 1866, and the mortality it occasioned in the three kingdoms was as follows :—

	Population, 1861.	Deaths from Cholera, 1866.
England and Wales,	20,066,224	14,378
Scotland	3,062,294	1,270
Ireland	5,764,543	2,501
		18,149

The distribution of this mortality in the several kingdoms is shown in the Appendix (Tables XXII., XXV.). The history of the diffusion of 1866 in England and Wales, elaborately written by Dr. William Farr, F.R.S., and enriched with much important matter relating to cholera, has been published as a supplement to the Registrar-General's 29th Annual Report.

The Diffusion in Europe, 1867.

1867.—Cholera continued more or less prevalent in many parts of Europe in 1867. The area of diffusion this year included, for the first time since the appearance of the disease on the south coast of the Continent in 1865, Switzerland, Dalmatia, Montenegrin, Albania, and Sardinia. Poland suffered generally from the year's diffusion, but 10 only of the governments of Russia in Europe were affected as compared with 55 in the previous year's diffusion. The disease was generally prevalent throughout Galicia, but elsewhere in the Austro-Hungarian Empire isolated outbreaks of no great magnitude, and limited to Hungary, Slavonia, and Dalmatia, appear alone to have occurred. No province of Prussia and of the Netherlands which had been affected in 1866 wholly escaped, but the incidence of the disease was slight as compared with that year. Several departments of France again suffered considerably. A hamlet in the vicinity of Cadiz was the scene of an isolated outbreak in Spain. In Italy cholera was more generally spread and more fatal in this year than in the two preceding years, Sicily suffering especially from the disease. Finally, an outbreak occurred in Switzerland, at Zurich, apparently an offshoot of the prevalence in Italy.* (*See* Map IV.).

Russia in Europe, 1867.

Russia in Europe.—Cholera first manifested itself in Russia in 1867, at the beginning of the year, in St. Petersburg. The diffusion of the previous year had ceased in that government on the $\frac{\text{30th November}}{\text{12th October}}$. The first case in 1867 occurred on the $\frac{\text{1st}}{\text{13th}}$ January, but the disease although it it did not entirely cease until the close of the year, never obtained any considerable proportions, for not more than 275 cases were

* In 1867 cholera was prevalent at several points of South America on the east coast, and in the interior, propagated there, it is stated, in the first instance, from the United States. The disease was carried from Rio Janeiro to the army in Paraguay, and it afterwards spread widely in the Argentine Confederation, and in the towns on both banks of the Rio de la Plata, Monte Video being last infected. Buenos Ayres suffered both in 1867 and 1868, about 6,000 deaths from cholera occurring from the appearance of the disease in 1867 to the end of February 1868. Cholera broke out at Belize, British Honduras, in December 1867, and extended to the neighbouring district and into Yucatan. (See an account of this last-mentioned outbreak by Staff-Assistant Surgeon Kearney, *Army Medical Department Report* for 1868, Vol. X., p. 317.)

recorded during the 12 months, and 139 deaths. Cases and deaths were reported in nine other provinces, namely, Vilna, Vitebsk, Volhynia, Grodno, Kovno, Kursk, Minsk, Riazan, and Kharkov, but in one only did cholera become largely prevalent. In Minsk there were 4,076 cases and 1,360 deaths from the $\frac{1}{13}$th June to the $\frac{6}{18}$th November. In Vilna 546 cases and 221 deaths happened, but in none of the other provinces did the cases and deaths reach these numbers. In Vitebsk the cases were only 65, the deaths 5 ; and in Riazan the cases and deaths were even fewer in number. The total number of cases reported in the several governments affected (all of which had suffered from the previous year's diffusion) was 6,245 ; the total number of deaths, 2,298. The distribution of these cases and deaths in the different governments is shown in the Appendix (*See* Table VIII.).

So inconsiderable was the manifestation of cholera this year in Russia, with the exception of the government of Minsk, that many medical men, Dr. Arkhangelsky states, believed that the disease recorded was principally *cholera nostras*.

Poland.—Dr. Arkhangelsky includes Poland in his account of this year's diffusion of cholera in Russia. The disease appeared at the same date (April $\frac{9\text{th}}{21\text{st}}$) in the governments of Warsaw and Lublin, and subsequently became prevalent in the other governments of the kingdom, although very slightly so in Lomjin and Souvalki, ceasing in Baletz on $\frac{20\text{th December 1867}}{1\text{st January 1868}}$. The total number of cases in the whole kingdom was 27,018 ; of deaths 11,265. (See *Appendix*, Table IX.)

Poland 1867.

Austria.—Galicia, the province bordering upon the infected districts of Poland and South-western Russia seems to have been alone affected with cholera in Northern Austria in 1867. The disease appeared in this province on the 3rd July 1866, and continued uninterruptedly until the 12th March 1867. Within this period there were 65,761 cases and 31,336 deaths among a population of 1,686,708. Certain counties of Hungary are stated to have suffered from cholera in 1867, few in number, but I have no definite information regarding them. The disease was reported to have broken out in Austrian Brood at the beginning of July. In Southern Austria cholera reappeared in Trieste, causing there, between the 15th August and 14th October, 366 seizures and 235 deaths ; and the disease now first seems to have manifested itself, during this epidemic, in Dalmatia and adjoining provinces. The district of Ragusa was attacked in June, the Herzegovina, within Austria, somewhat later. Numerous villages were affected and several of the largest towns, but the disease, although widely diffused, did not as a rule show itself (so far as an opinion may be formed from imperfect details) in these localities with any great intensity. At the time that cholera was prevalent in this portion of the Austrian Empire, it was prevalent also in Turkish Herzegovina, Montenegrin, and Northern Albania.

Austria, 1867.

Prussia.—The diffusion which began in Prussia in February 1866, continued uninterruptedly until the middle of February 1867, when it ceased for the moment, having lingered longest in the province of the Rhine, within the government of Dusseldorf. The return given by Dr. Engel for 1867, (the only one relating to this year which has yet come under my observation,) is imperfect, not including the records for the city of Berlin, and the governments of Königsberg, Posen, Magdeburg, Minden, and Kiel. So far as this return goes, it would appear that the disease reappeared, in March, in the governments of Coblenz and Treves,

Prussia, 1867.

Rhenish Prussia, and subsequently in other provinces; and after continuing to the close of the year it died out altogether. In one district only, the government of Dusseldorf, was this year's prevalence as considerable as that of 1865. Elsewhere the incidence of the disease was slight. The total number of seizures of cholera recorded among the civil population during the year was 11,173, of deaths from the disease 5,797, the corresponding figures for the previous year being 224,382 and 114,683. In 1867 the returns included the provinces annexed to Prussia in 1866, namely, Schleswig-Holstein, Hanover, Hesse-Nassau, and Lauenburg. Of the state of cholera in these provinces in 1866, (if there were any prevalence of the disease within them in that year,) I have no knowledge. The total seizures from cholera in these provinces in 1867 were 332; the total deaths, 234. The following is a summary of the distribution of the sickness and mortality from cholera in the kingdom in 1867. A more detailed statement is given in the Appendix (*See* Table XXVIII.).

Prussia.—Cholera, 1867.*

Provinces.	Civil Population, 1864.	Cholera.		Duration of Diffusion.
		Attacks.	Deaths.	
Prussia	3,014,595	1,551	910	14 June - 30 November.
Posen	1,523,729	124	53	14 July - 13 October.
Brandenburg	2,616,583	15	7	9 „ - 15 „
Pomerania	1,437,375	1	1	25 „ - 25 „
Silesia	3,510,706	2,053	1,110	6 April - 8 November.
Saxony	2,043,975	422	103	6 September - 16 „
Westphalia	1,666,581	330	195	12 August - 28 December.
Rhine	3,346,195	6,677	3,418	1 January - 20 „
Hohenzollern	64,958	—	—	
Jahde	1,573	—	—	
Schleswig Holstein	960,996	4	4	28 August - 6 September.
Hanover	1,923,492	308	217	27 „ - 21 October.
Hesse-Nassau	1,203,297	20	13	17 May - 8 December.
Lauenburg	49,704	—	—	
		11,505	6,031	? January - 28 December.

Montenegrin.—Cholera appeared in Montenegrin about the beginning of July. It had been preceded by famine and very fatal typhus, and, spreading throughout the principality, it was very virulent in several localities.

Turkey.—The starting point of this year's outbreak in Turkey, which included in its area Montenegrin, the Herzegovina, and Southern Dalmatia, would appear to have been in Northern Albania. Cholera was reported to be present at Rici, a village on the River Bojana, in this province, in April. Other villages in the neighbourhood were affected, but the outbreak here was circumscribed and the disease disappeared in May.

Italy.—Beginning in 1865, continuing and becoming more widely prevalent in 1866, the epidemic culminated in Italy in 1867, and is

* Exclusive of the City of Berlin, and the Governments of Königsberg, Posen, Magdeburg, Minden, and Kiel.

reported to have come to an end on the 15th January 1868. Forty-five provinces had been affected in 1866; fifty-five were affected in 1867. The mortality which in 1865 (exclusive of Venetia) had been 12,901, in 1866 (now and in the following year, including Venetia) was 19,571, and in 1867, 128,075 [? 127,775]. The provinces which chiefly suffered from cholera in 1867, were those of the island of Sicily, where the mortality was enormous (nearly one half, 54,107, of the whole named deaths occurring there); and on the mainland Bergamo, Brescia, Capitanata, Como, Cremona, Genoa, Milan, Naples, Novara, Parma, Piacenza, Terra di Bari, Terra d'Otranto, and Turin. (See *Appendix*, Table XX.). Sardinia, which had escaped the two previous years, came within the area of the diffusion this year. According to local reports,* cholera appeared in the island, at Cagliari in the month of August, and spread to the district of the same name, and to the district and town of Iglesias, continuing throughout the months of September and October and ceasing in November. In the city of Cagliari (population, 1862, 28,244), there were 160 deaths: in the district (population, 30,905) 174 deaths, the total number of the cases in the city and district being 843. In the town and district of Iglesias (population, 1862, 6,224) there were 814 cases and 230 deaths (142 town and 88 district). The total number of cases in the island was 1,657, of which 564 were fatal.

Sardinia, 1867.

The following is a summary statement of the mortality from cholera in Italy during the three years 1865, 1866, 1867, and of the progress of the mortality from month to month in the several years, according to the general official reports previously referred to:

Italy.—Cholera, 1865, 1866, 1867.

	Population, 1862.	Deaths from Cholera.		
		1865.	1866.	1867.
Italy { Continental	18,797,087	12,901	12,298	73,403
Italy { Sicily	2,391,802	—	7,273	54,107
Italy { Sardinia (Island of)	588,064	—	—	565
Total	21,776,952	12,901 [? 12,885]	19,571	128,075 [?127,775]

Sicily, 1866-67.

Sicily.—Provinces.	Population, 1862.	Deaths from Cholera.	
		1866.	1867.
Caltanissetta	223,178	60	7,209
Catanea	450,460	687	12,053
Girgenti	263,880	98	12,516
Messina	394,761	6	4,483
Palermo	584,929	5,688	12,533
Syracusa	259,693	—	2,353
Trapani	214,981	734	3,160
Total	2,391,802	7,273	54,307

* *Sul Colera Asiatico che domino in Diversi Comuni della Provincia di Cagliari nel* 1867. Relazioni Storiche del Cav. Dott. Giovanni Falconi. Cagliari, 1868.

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Europe, 1867.

Italy.—(Months).	Deaths from Cholera.			
	1865.	1866.	1867.	1868.
January - - -	—	93*	888	107
February - - -	—	53*	362	—
March - - -	—	8*	808	—
April - - - -	—	2	693	—
May - - - -	—	1	2,421	—
June - - - -	1	3	22,962	—
July - - - -	576	76	39,256	—
August - - -	7,673	1,054	33,655	—
September - - -	3,520	5,918	16,509	—
October - - -	3,566	6,595	6,449	—
November - - -	6,633	4,945	2,229	—
December - - -	1,444	965	736	—

I have but one piece of information respecting cholera in the States of the Church in 1867. Cholera appeared in Rome on the 1st May, and from that date to the 20th October there were 3,024 seizures and 2,040 deaths.†

Malta, 1867.

Malta.—There was a slight reappearance of cholera in Malta this year (1867). Two women from Turin, and the captain of an Italian vessel died of the disease, at the beginning of July, in the lazaretto, Valetta:—"About the same date there were a number of cases of choleraic "diarrhœa among the civil population in some of the villages, and one "severe case was reported in the 64th Regiment at Zabbar Gate "Barracks. No further case of cholera occurred till the 23rd of "August, when a woman, residing at Valetta, was attacked and died "after 73 hours' illness; and several cases of choleraic diarrhœa, some "of which proved fatal, were reported among the civil population. On "the 30th August the 1st Battalion, 14th Foot, arrived at Malta from "Ireland, and six companies were immediately sent to Pembroke Camp, "getting thoroughly drenched by a storm on the line of march. The "same night a fatal case of cholera occurred at the camp in the wife of a "private of the 1st Battalion, 60th; a woman who in consequence of her "bad character had been struck off the strength of the regiment. On "the 2nd of September, a man of the 14th was attacked, and died in "$9\frac{1}{2}$ hours." Other cases followed among the troops in the camp, and elsewhere in the island, and 22 men died of the disease, 15 in September, 5 in October, and 2 in November. The deaths from cholera among the families of the soldiers during the same period were eight, four women and four children.‡

* The numbers for these months are taken from the Official Report for 1865. In the Official Report for 1866–67, the numbers are given as follows:—January, 5; February, 5; March, 2.

† Dr. Francesco Scalzi.—*Il Colera di Roma sul* 1867. Roma, 1868.

‡ The following is of interest with reference to contemporary prevalence of cholera in the Regency of Tunis:—The first person attacked with cholera in Leghorn (where from the 13th July to the 15th November there were 1,275 cases and 824 deaths), was a widow woman whose seizure occurred under the following circumstances:—In her house at the time of seizure a Tunisian family was lodging which had fled from Tunis in consequence of the prevalence of cholera there. Thirteen days after this family had landed, and after it had been subjected to quarantine, a child sickened from diarrhœa. The child was nursed by the widow, who while having it in charge was seized with cholera during the night of the 13th–14th July, and died in 24 hours. The other persons in the house, including the Tunisian family, all suffered afterwards with choleraic diarrhœa, and the child first seized died after a short illness.—*Relazune della Commissaire Municipale di Santà sul Colèra di Licorno.*

‡ Army Medical Department Report for 1867. Vol. IX., p. 49.

Switzerland.—The outbreak which occurred in Zurich in 1867 is believed to have been an offshoot from Italy. A family coming from Rome, and bringing with them a child suffering from diarrhœa, is held to have introduced cholera into Zurich during the last week of July. After that period cases began to occur in the city and vicinity; and from the 3rd August to the 10th October, 428 deaths from cholera were reported. Cases of the disease were stated at the time, but on doubtful authority, to have taken place also at Lausanne and elsewhere in Switzerland. *Switzerland, 1867.*

Spain.—At the end of October an outbreak of disease described as choleraic took place at San Fernando, a village situated on the coast six miles distant from Cadiz. 20 cases, of which 14 died, occurred within a few days. *Spain, 1867.*

France.—Cholera had not ceased in the departments of Pas-de-Calais, Côtes-du-Nord, and Ille-et-Vilaine at the end of 1866. In 1867 the disease continued in those departments and reappeared in others. According to the Report on Epidemics presented to the Academy of Medicine,* which, as already explained, refers solely to information on the subject communicated directly to the Academy, the disease in 1867 showed itself in 11 departments, and in these was distributed in 134 communes of 28 arrondissements, and caused 2,783 deaths. The departments affected and the distribution of the mortality in them were as follows:— *France, 1867.*

Department.	No. of Communes affected.	Deaths from Cholera.
Pas-de-Calais	20	116
Côtes-des-Nord	11	900
Ille-et-Vilaine	26	510
Charente-Inferieure	6	31
Finistére	11	676
Meurthe	4	20
Morbihan	21	159
Seine-et-Oise	2	25
Savoie	28	308
Nord	1	35
Ain	4	3

The Netherlands.—The epidemic is credited with 1,595 deaths in the Netherlands this year. Of these 1,033 occurred in the province of South Holland. The remainder were distributed in other provinces as follows:—Gelderland, 50; North Holland, 219; Zeeland, 48; Utrecht, 27; Friesland, 19; Overyssel, 4; Groningen, 3; Drenthe, 21; North Brabant, 102; Limburg, 69. *The Netherlands, 1867.*

Bavaria.—Cholera is reported to have broken out at Friesenheim (population 1,800) near Manheim, in August, and afterwards to have prevailed in several villages of Rhenish Bavaria. *Bavaria, 1867.*

1868.—This year cholera, so far as is known, manifested itself in an epidemic form in two localities only in Europe, namely, in the district of Lipowetz, government of Kiev, Russia, and in a valley on the River Rour, near Relinghausen, in Essen, Germany. In the district of Lipowetz the *The Diffusion in Europe, 1868.*

* *Mémoires* t. xxi.

settlements of Great Rostowka and Sollogoubowka were attacked, and 70 cases of cholera, of which 29 died, occurred in them from the 10th August to the end of the month. Thirteen isolated cases of cholera occurred in other parts of the province of Kiev, of which six were fatal. The total mortality from the disease within the province, from the 10th to the 27th August, was 35. The commencement of the outbreak in Germany is also dated the 10th August, and from that day to the 4th September there were 38 deaths from cholera in the locality which has been referred to.* *See* Map IV.

There was was no prevalence of cholera in the government of Kiev in 1867, but the disease was active in the adjacent governments of Minsk and Volhynia, inconsiderably so in the latter government, but causing 4,076 cases and 1,360 deaths in the former.

Dr. Arkhangelsky makes the following observations on the occurrence of cholera in Russia in 1868 :—

"Besides the cases referred to [in the government of Kiev], isolated cases of cholera happened during the hot season of the year in many provinces of Russia, but the medical men attributed such cases to sporadic cholera (*cholera nostras*). The greatest number of these cases were observed in the city of St. Petersburg (92 cases, 56 deaths), in other parts of the province of St. Petersburg (88 cases, 42 deaths), and in the city of Moscow (47 cases, 14 deaths). In general, however, sporadic cholera (*cholera nostras*) appeared oftener in the western parts of Russia, where the total number attacked by the disease reached 400, and the deaths from it 130. In the central and eastern districts the number attacked by *cholera nostras* was 150 and the deaths were 28.

"Was the epidemic in the province of Kiev really Asiatic cholera and not sporadic cholera (*cholera nostras*), as in the other provinces? or was the disease in the other provinces also Asiatic cholera occurring in isolated cases? These questions cannot be solved with certainty. The great number of cases of assumed sporadic cholera in the western part of Russia, and the number of deaths caused by the disease there at once arrest the attention and lead to a suspicion that the diagnosis of the local medical men was not accurate. But an examination of the climatic conditions of 1868 makes it probable that the cases in question were really not of specific origin. According to Mr. A. Voiekov the summer of 1868 was remarkable for the contrast in the distribution of rains in the western and eastern parts of Russia. At St. Petersburg, during the whole summer there were only 1·14 inches of rain, instead of the usual 6·56 inches. This drought spread itself eastwards to Kostromo, and southwards to Nikolaiev and Lougani, where the months of May and June were especially very dry. The forests lying between Nijni-Novgorod and the Prussian frontier were in July much damaged by fires which destroyed great quantities of trees. In the eastern part of Russia it was just the contrary. At Kosmodemiansk, in the province of Kasan, the rainfall in July was 4·03 inches above the average quantity. At Orenburg the months from May to September were unusually wet. Along the whole lower bank of the Volga a splendid harvest followed the timely rains. The Caucasus also came within the area of the unusual rainfall. At Tiflis, April, August, September, and October were particularly wet.†

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* I am indebted to Dr. Arkhangelsky's work for the details of the outbreak in Germany, as well as of the outbreak in Russia.

† A. Voiekov on the Distribution of Rains in Russia.—Meteorological Transactions (Russian), Vol. I., pt. 2. St. Petersburg, 1870.

"I think that the meteorological conditions here described are sufficient to account for a local origin of the cases of cholera occurring sporadically in Western Russia this year, and even for the isolated cases which were observed in the province of Kiev. But the relatively considerable prevalence of cholera in two adjoining villages of that province cannot be reasonably explained in this manner. Moreover, the development of cholera in the province of Kiev and other provinces the following year (1869), proves the existence of the specific cholera agent in the province of Kiev in 1868."

The development of cholera here mentioned by Dr. Arkhangelsky, refers to that recurrence of the disease in an epidemic form in the province of Kiev in 1869, which proved to be the beginning of another diffusion in Europe, almost if not altogether as considerable as that which began in 1865. This development will be a subject for separate consideration in another part of this report (Sec. IV). With the slight reappearances of cholera which occurred in Russia and Germany in 1868, the diffusion which began in Europe in 1865 virtually ended. I now, therefore, having completed this part of my subject, proceed to describe, before tracing out the other lines of diffusion along which cholera travelled in spreading from Alexandria in 1865, the several secondary diffusions from Europe, to Asia, to America, and to Africa.*

2.—*The Diffusion to the South and East Coasts of the Black Sea.*

North-east and Eastern Anatolia, 1865.

When in 1865 the scattering of cholera began from Constantinople to the west coast of the Black Sea, it began also to the south coast. Many persons sick from cholera, or corpses of persons who had died of cholera, were carried in the ordinary course of traffic by ships sailing from the Bosphorus into Sinope, Samsun, Trebizond, and Batum. The details of the importations into the ports and lazarets at Sinope and Batum are not known; but into Samsun 15 persons sick of cholera, and the corpses of 11 persons who had died at sea from the disease, and into Trebizond one sick person and six corpses were brought between the 25th July and the 28th August. At one only of the ports referred to did the disease extend to the population of the town, namely at Trebizond. Here the permanent lazaret was not capacious enough for the number of persons who were subjected to quarantine in it, at one period amounting to 600 under detention at the the same time, and it was necessary to camp out many in tents. Cholera broke out both in the permanent lazaret and in the encampment, and caused not less than 39 deaths. The vessel which brought the single case of cholera into the port, and landed it at the lazaret, arrived on the 25th July. Before this date cholera did not exist in the town, and had not been observed among the shipping. Soon after the arrival of this vessel a case of cholera, described as sporadic, was observed in the town, and from the beginning of August to the middle of September, 46 cases, of which 28 were fatal, happened there.

Armenia, 1865.

From Trebizond cholera was dispersed in two directions, one into Armenia the other into Caucasia. A body of Kurd and Armenian labourers coming from Constantinople, and passing through Trebizond,

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* The year 1868 is remarkable for the seemingly wide occurrence of dearth in Europe and Northern Africa. Dearth is noted among papers before me in parts of Finland, Bothnia, Sweden, Norway, East Prussia, Hanover, Nassau, Galicia, Spain, Portugal, Algeria, and Tunis. In Algeria and Tunis the dearth was accompanied by wide-spread and very fatal typhus. There was dearth also in Siberia.

carried the disease to Erzerum, where it appeared on the 22nd August, and where from that date to the 12th December it attacked 517 persons, of whom 224 died. During its prevalence in that city 600 Tchetchen families coming from Cis-Caucasia, who passed through it seeking for a settlement in Diarbékr, contracted the disease, and carrying it with them infected Mush, a town situate about 80 miles south of Erzerum. Then returning to Erzerum, these families sought re-admission into the Russian Empire, and travelling by way of Kars to the frontier, they carried cholera into that town. Both in Mush and in Kars, but few cases of the disease occurred, and during the winter it apparently died out altogether in Armenia.

Caucasia, 1865-67.

Cholera was imported into Caucasia by a body of Greek emigrants coming from Trebizond, one of whom, the first case recorded, was attacked at the fort of Novorossiisk on the $\frac{28\text{ July}}{9\text{ August}}$. The day following a non-commissioned officer was attacked on board a Russian schooner, anchored in the roadstead.* During the next four days nine fatal cases of cholera occurred in the fort.

On the $\frac{6}{18}$th August, a sailor was attacked with cholera on board the Russian corvette "Yastreb," which had arrived off Sukhum from Novorossiisk. The day following another case occurred on board. This case was sent into the hospital of Sukhum. There the disease spread to other patients, and cases also occurred in the town.

On the $\frac{12}{24}$th August cholera appeared in the hospital at Poti, and extending along the valley of the Rion, it broke out at Kutais on the $\frac{19}{31}$ August. At this time the works of the Poti-Tiflis Railway were in progress, and the men engaged upon them were encamped in various parts of the valley. The disease attacked these encampments and clung to them with great tenacity. In Kutais the disease prevailed until October, when it apparently ceased; but in the month of November, when a large number of peasants from the neighbouring districts, especially from Kulamey, had congregated in the town on the occasion of the promulgation of the Emperor's edict, relating to the liberation of serfs, cholera reappeared, and was dispersed in the surrounding country by the returning peasants. The disease persisted in Kulamey and Gori until December, but in neither place nor in Suram, which was also infected, were the cases numerous.

On the $\frac{25\text{ August}}{6\text{ September}}$ cholera appeared in Tiflis. The persons first attacked were a Frenchman and his wife, who journeying by way of Poti and Kutais, where cholera existed at the time, reached Tiflis on the $\frac{23\text{ August}}{4\text{ September}}$. From the $\frac{25\text{ August}}{6\text{ September}}$ to the $\frac{1}{13}$th November there were 353 cases, of which 116 were fatal, in this city. On the $\frac{6}{18}$th September there was a second importation of cholera into Tiflis. Certain battalions of the army of reserve, which had marched to Tiflis by the military road, reached the city with cholera in the ranks. Among these troops 221 cases and 118 deaths occurred.

On the $\frac{1}{13}$th October cholera appeared in Erivan, and during the same month it broke out at Nakitchevan, and in the district of Elizabethpol. In Erivan the first case occurred among the military, and the disease is believed to have been introduced by two detachments of troops coming from Tiflis; but both in this town and in Nakitchevan there was a

* By an unfortunate misprint these dates of the cases are given in the report of the International Sanitary Conference of 1866, ("Sur la Marche," &c.), as the 28th and 29th *June* instead of the 28th and 29th *July* (*O.S.*), and the error is complicated by the fact of the Old Style being retained without reference to the fact. The account of the introduction of cholera into Caucasia, and of its subsequent extension there, is derived from the report referred to and from Dr. Arkhangelsky's work.

probability of infection, it would appear, from Persia. From the $\frac{1}{12}$th September to the $\frac{5}{17}$th December, there were 392 seizures and 100 deaths from cholera among the civil population, and 118 cases and 35 deaths among the military. The disease extended into the districts of Novo-Bayazid and Eckmiadzine, and there, as also at Nakitchevan, it prevailed with much severity.

In November, cholera ceased at Tiflis, and a month later, according to information communicated to the International Sanitary Conference, 1866, by Dr. Bykow, one of the Russian delegates, it disappeared from Caucasia, "sans avoir laissé nulle part, à ce qu'il parait des traces de foyer secondaire."

The following year (1866) cholera, however, again appeared in Caucasia, but very little seems to be known of its prevalence there at this time. Dr. Arkhangelsky merely says: "Speaking generally, the "manifestation of cholera in Caucasia was weak. In the government of "Stavropol the number of cases was 1,273; the number of deaths, 403; "on the coast of the Black Sea, in the Kuban district, the number of "cases was 1,421, of deaths 295. The numerical data for other districts "of Caucasia are not known, but according to Dr. Rouchevsky the "number of persons attacked was small in comparison with former years "of prevalence."

Dr. Arkhangelsky does not refer to the prevalence of cholera in Caucasia in 1867, but the disease was present in at least one locality. On the $\frac{2}{14}$th August it broke out at Hassav-Yourt, in the district of the Terek, and from that date to the $\frac{1}{13}$th September it attacked 481 persons, of whom 210 died.* (*See* Maps II.–IV.)

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* *Transactions of the Imperial Medical Society of the Caucasus*, 1867. The following is an extract from Dr. Kozlovsky's article, entitled "Cholera in the Fort of Hassav Yourt (province of Ter) in 1867."

"Cholera visited the fort Hassav-Yourt in the beginning of August 1867. The first case of cholera known to us at Hassav-Yourt was that of a military student Ivan Fedorovsky, aged 15, who, on the way between the fort Cheer-Yourt and Hassav-Yourt, ate some raw berries, and drank a great deal of water. On his entering the military hospital here we found in him all the symptoms of cholera. He recovered on the $\frac{1}{13}$ September. From that date, the $\frac{2}{14}$ of August, soldiers of the marching battalions were received daily at the hospital, and their number gradually increased. In a week we began to consider the cholera fully developed. The following table gives a list of the patients in the cholera-ward at Hassav-Yourt for the first seven days of its existence.

—	In the hospital.	Received.	Cured.	Left.	Deaths.	Remain.
Old Style.						
2nd August - -	0	4	—	—	—	4
3rd „ - -	4	49	—	—	—	53
4th „ - -	53	43	—	—	1	95
5th „ - -	95	86	—	1	4	176
6th „ - -	176	59	—	2	5	228
7th „ - -	228	63	—	—	19	272
8th „ - -	272	31	26	—	25	252

"Cholera at Hassav-Yourt did not in any way differ from the known epidemics which I had to watch in 1847 and 1848 in the town of Kiev, in 1855 at Kars, (in Asiatic Turkey), in 1857 in the fort of Grozni (in the Caucasus), or from the epidemic of last year (1866) at Tiflis and many places of the Transcaucasian country.

"We must consider that the cholera is brought here (to Hassav-Yourt) by the marching battalions. We had no cholera here last year, notwithstanding that it appeared in Caucasus and in the Transcaucasian country, and reached Tiflis, because the communications between Hassav-Yourt and the above countries are rare.

The Diffusion to the West Indies and North America.

The appearance in the Leeward Islands, 1865.

While the eastward diffusion from Europe to Asia Minor and Caucasia was in progress, a westward diffusion across the Atlantic to the Leeward Islands and the American Continent began.

Guadeloupe.

The Leeward Islands.—Guadeloupe.—Cholera appeared here on the 22nd October 1865, in the town and port of Point-à-Pitre. The history of the first occurrences of the disease, with reference to the question of introduction from without, was not inquired into at the time; the local authority maintaining that the malady was a form of paludal fever ("une fièvre paludienne, la fièvre pernicieuse algide")* of local origin, and withholding information necessary for an accurate examination of the question. On the 9th October, a sailing ship, the "Virginie," 36 days out from Marseille, had arrived at Point-à-Pitre and begun to discharge her cargo. She carried no passengers, and the health of the crew, numbering 12 to 15 men, had not suffered, it is stated, any disturbance during the voyage. The ship had left Marseille on the 3rd September, when cholera was prevalent there, and it was at first suggested that she had in some way been the carrier of the disease.

Another source of communication has been suggested by Dr. Pellarin, a retired medical officer of the French Marine, who witnessed the outbreak, and who made such investigation of its early history as was possible under the difficulties raised by the local government. He has published the results of his researches in a work of great interest relating to the medical topography of Guadeloupe and the hygiene of tropical countries †. According to Dr. Pellarin the person first attacked at Point-à-Pitre was a negro, a rope-dancer by occupation. He was attacked during the evening of the 22nd October while engaged in a public performance, and died in the course of the night. It was reported that shortly before his seizure he had visited twice, if not more frequently, a ship, the "Sainte Maire," which, bound for Mexico, had put into Point-à-Pitre on the 20th October, 36 days out from Bordeaux, where, at the close of summer, there had been some extension of the

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" The following table shows the number of cholera patients in the fort Hassav-Yourt during 42 days.

In the hospital.	Received.	Cured.	Left or transported.	Dead.	Remain.
August 2nd to the 9th - - 0	335	26	3	54	252
„ 9th–16th - - 252	63	22	2	94	107
„ 16th–23rd - - 197	47	81	3	40	120
„ 23rd–30th - - 120	14	41	8	10	75
„ 30th—Sept. 6th - - 75	16	27	4	5	55
September 6th–13th - - 55	6	33	4	7	17
Total during 43 days - -	481	230	24	210	17

" From these cases we have to deduct several having merely diarrhœa, thus limiting the real cholera cases to 357; of these only 147 recovered, *i.e.*, 41·2 per cent.; the number of deaths is 210, *i.e.*, 5·88 per cent."

* Reply of the Governor of Guadeloupe to an inquiry of the Lieutenant-Governor of Dominica, dated 5th Nov. 1865.

† *Hygiène des Pays Chauds.—Contagion du Choléra demontrée par l'Épidémie de la Gaudeloupe. Conditions Hygiéniques de l'Emigration dans les Pays Chauds et de la Colonisation de ces Pays.* Par A. Pellarin, M.D., Médicin principal de la Marine en retraite. Paris, 1872.

epidemic of cholera then prevailing in many parts of France. This ship had lost one of her crew at sea on the 9th October from an undefined illness of twenty-two days' duration, as stated by the master. The negro returning from one of his visits to the ship carried with him a packet of dirty linen, for the purpose of being cleansed, to a washerwoman named Scolastique. She was attacked with cholera on the 25th October and died the same day. On the 25th, also, a negro lad, 12 years old, who had visited the rope-dancer more than once during his short illness, was attacked and died in seven or eight hours. Then four washerwomen, associates with Scolastique, and working with her in the same wash-house, were attacked in quick succession, one on the 27th October, one on the 28th, the third on the 31st, and the fourth at the beginning of November, and all died. The washerwoman attacked on the 27th October was the fourth person who suffered from the disease. But from the date of her seizure other cases, as well as those of the three other washer-women, began to occur quickly in the neighbourhood where she worked and lived, including relations and friends of those persons who had already been attacked with the disease. Cholera spread throughout Guadeloupe and did not cease until the month of April 1866, the last death being recorded on the 16th in the commune of Moule. During the six months of its prevalence it caused 11,957 deaths, among an estimated population of 149,407.

Dominica.—Dominica did not entirely escape, in 1865, the introduction of cholera into the Leeward Islands, but the cases which occurred there were imported, and the population of the island appears to have been unaffected. The circumstances of the introduction, as gathered from a despatch of the Lieutenant Governor, dated the 23rd April 1866, are thus related by the Medical Officer in his Ninth Report (p. 26) :— *Dominica*, 1865.

"Dominica is 22 miles from the main island of Guadeloupe, but only 15 from some of its dependencies, certain small islands called 'Marie-Galante,' and 'Les Saintes.' Up to the beginning of November 1865 the communications between these small islands and the north end of Dominica was constant, almost daily; the markets of Marie Galante were supplied with provisions and vegetables from Dominica, and carpenters, bricklayers, and others living in Dominica went across the narrow channel to work at Marie Galante, leaving their wives and families at home. It was on the 2nd of November that a rumour reached Dominica that cholera had broken out at Point-à-Pitre, in Guadeloupe. On the 4th the Lieutenant-Governor of Dominica sent to the Governor of Guadeloupe for information; and feeling persuaded after the return of the messenger that it was an outbreak of cholera, he on the 9th declared Point-à-Pitre in quarantine. Afterwards, when news arrived that the disease was spreading through the island of Guadeloupe, the whole of the island and its dependencies were placed in quarantine. Despite this precaution, a boat from Marie Galante, filled with persons, some still healthy and some sick with cholera, succeeded in reaching Dominica. A strict guard was placed by the Lieutenant-Governor on the village at which these persons had landed, and for the future "health guards" with loaded muskets were stationed at every place round the island where landing was possible, to prevent persons from Guadeloupe from setting foot on the island. These measures of precaution were entirely successful, and, so far as I can gather from the despatch, only two persons died of cholera in Dominica, and these were two boatmen who landed from the boat mentioned above, and died on the beach, close to the village that was subsequently isolated."

The appearance in New York, 1865.

The Continent of America.—On the 10th October 1865, the "Atalanta," an English mail steamer, sailed from London, bound for New York, with a full cargo and 40 passengers, 28 cabin and 12 steerage. The next day she put into Havre, remained there one day, and received 24 additional cabin passengers and 540 steerage passengers. These persons came chiefly from Switzerland, Germany, and Eastern France. Almost all had passed through Paris on their journey to Havre, and some had stayed there several hours, others several days. At the time cholera was rapidly increasing in Paris, the month of October being the month of greatest prevalence in that city in 1865. In Havre cholera was first reported on the 18th October, and 19 deaths altogether occurred in the commune, according to the official returns. Some of the emigrants while at Havre were taken ill, and were visited and attended by Government officials. One woman died there, and Dr. Swinburne, the health officer for the port of New York, from the account of the symptoms given to him by her husband, was convinced that she had succumbed to cholera. The "Atalanta" sailed from Havre on the 12th October with a clean bill of health. On the 13th a child died from cholera on board. On the 14th, 16th, 18th, 19th, and 22nd a death from cholera occurred each day (five altogether) in one family, who, while at Havre, had stayed in the same hotel where the woman, previously referred to, had died. The ship arrived at New York on the 2nd November, when the surgeon reported 60 cases of cholera and eight deaths during the passage. The vessel was subjected to a strict quarantine, during the continuance of which 42 other cases took place and eight deaths.

Twenty days after the arrival of the "Atalanta" at New York, and eight days before this ship was released from quarantine, cholera appeared among the patients in the State Emigrant Hospital, on Ward's Island. The first person who suffered here was attacked on the 22nd of November. Other attacks followed, and from that date to the 20th December, when the disease ceased, there were 31 cases, of which 27 died. In the official report* on this outbreak no information is given as to the date of arrival of the persons attacked in New York, nor of the ships which had brought them, nor of the ports whence they had sailed. "Nearly all the cases," states Dr. George Ford, the principal physician of the hospital at the time, "occurred in the same building; nearly all were "women and children, as the building was appropriated to patients of that "class, and nearly all were labouring under acute disease or were con-"valescent from it." The appearance of cholera had been preceded by much diarrhœa and dysentery.

From the cessation of this outbreak until the 1st May 1866 no other occurrence of cholera was recorded in the city and suburbs of New York.

Ward's Island, which contains the New York State Emigrant's Refuge and Hospital, is situated 18 miles, or thereabouts, in a direct line from the quarantine anchorage in Lower Bay, where lay the "Atalanta" and the quarantine receiving and hospital ships. It appears to be quite certain that no communication could have taken place between the sick on Ward's Island and the infected crews and passengers and the sick at the quarantine station, during the 28 days that the latter were subjected to detention. Whatever the source from which the disease had originated in the Emigrant's Hospital, it could not, according to the evidence adduced, have had connexion with the "Atalanta," although the outbreak occurred not long after the arrival of that vessel.

* *Report of the Metropolitan Board of Health, New York*, 1866. Appendix M., p. 424.

Before the outbreak on Ward's Island had come to an end, another infected ship had arrived at New York, the "Mary Ann," an American barque, which had sailed from Havre on the 25th October. She reached her destination on the 12th December, and the captain reported five deaths among the crew and passengers during the passage, four from cholera.

The appearance in New York, 1866.

No other importation of cholera into New York harbour took place until the 18th April 1866 when the steamship "Virginia," 2,936 tons, arrived in the Lower Bay, with 46 passengers sick of the disease on board. This ship had sailed from Liverpool for New York, on the 4th April. She touched at Queenstown to complete her complement, and when she left that port had on board 1,033 passengers (14 cabin and 1,019 steerage), her crew consisting of 110 men. Of the steerage passengers, 220 were German, Dutch, Danes, and Swedes, the remainder Irish, English, and Scotch. On the 12th April, the eighth day after the ship had left Liverpool, a steerage passenger, named Peter Voss, coming from Groningen, in Holland, died of cholera. This man had had several days' diarrhœa before the fatal seizure occurred and the nature of his malady was recognised. He had joined the ship at Liverpool, having travelled from his home to that port, with his family, by way of Amsterdam, Rotterdam, and Hull, leaving Groningen on the 29th March. Cholera was not known to be present in any of the places through which he passed at the time of his journey, but its appearance in Rotterdam was officially recognised on the 8th April, about a week, or probably even a less time, after he had been in that city. From the 12th to the 18th April, the date of the ship's arrival at New York, 33 of the passengers and two of the crew had died of cholera, and, as already stated, 46 passengers were ill of the disease when she reached her destination. During the detention of the passengers 46 days in quarantine, 144 other cases occurred among them, making altogether 190 cases received into the hospital ship. Of these cases 72 died, the whole number of deaths, from the commencement of the vessel's voyage from Liverpool to the termination of the quarantine at New York, being 110.*

Two days after the "Virginia" had reached New York the steamship "England" arrived in the harbour. She had no cases of cholera on board at the time, nor did any cases occur among the crew and passengers during 20 days' detention in quarantine. But many cases had occurred at sea, rendering it necessary for the ship to put into Halifax, Nova Scotia, and there the disease was communicated from the ship to the shore in several instances of remarkable interest.

The steamship "England," 3,440 tons burthen, bound for New York, sailed from Liverpool on the 28th March 1866. She carried from the Mersey 16 cabin, and 791 steerage passengers, and had a crew of 122 officers and men. Touching at Queenstown on the evening of the 29th, she received on board there, in addition, 1 cabin, and 393 steerage passengers, and put to sea again as soon as the embarkation was effected. The total number of persons at that time on board the ship was 1,322. Of the passengers who joined the "England" at Liverpool 465 were emigrants from the Continent of whom the precise

* *Report of the Commissioners of Quarantine Health and the Officer of the port of New York* (Dr. John Swinburne) for 1866. I have adopted the figures given in Table B. of this Report (p. 71). There are certain discrepancies between this Table and the text of this Report. I have adopted also the statement made in this Report respecting the number of foreigners among the passengers on board the "Virginia," namely, 220, in place of the number (465) given in a previous Report of mine, to which reference is made (p. 64).

nationality was not known. Some were German, some probably Dutch, and many, if not the greater number, had left the Continent by way of Rotterdam, where cholera soon after (8th April) was recognised in the city. On the fourth day after the ship had left Queenstown (the 2nd April), early in the morning, a German lad, eight years old, was found dead in the fore-steerage, in his mother's berth, and was believed to have died from cholera. The same day an Irishman was seized with fatal cholera. From this date to the 9th April, when the ship put into Halifax, there were 150 cases of cholera, of which 46 died, six of the fatal cases being among the crew. The sick were removed to a hulk, the seeming healthy to tents erected on an island in the harbour, but the disease continued unabated for several days, not less than 200 deaths occurring in addition to those which had happened on board. Comparing the number of passengers and crew who ultimately reached New York, or could otherwise be accounted for, with the number who were on board at the time the ship left Queenstown, 256 were missing, and this number probably represents the total mortality. The disease, it is stated, was more prevalent among the German than among the other, chiefly Irish, passengers.

Several of the emigrants escaped from quarantine and gained the mainland, but in no instance do they appear to have communicated cholera to the population. On the other hand, there were examples of such communication among persons who had direct or indirect relations with the ship or passengers. The medical officer of health for the city and port of Halifax, Dr. Slater, in the discharge of his duties, contracted cholera on the 16th April, and died after 17 hours' illness. The pilot who brought the "England" into the harbour, and an assistant, also contracted cholera, and transmitted the disease to others. Several cases of cholera, moreover, occurred apparently in connection with infected bedding from the ship. The circumstances under which the pilot and his assistant contracted the disease were of singular interest, and together with the apparent communication by infected bedding, were made the subject of special investigation by Deputy Inspector-General Barrow, the principal medical officer at the time of the forces in Halifax. I give his graphic and instructive account: —

"At break of day on the 9th of April, a pilot named Terence was in his open boat, lying off Cape Sambro, five miles north-east from Sambro Island, and about 15 miles from Halifax. An assistant named Purcell and his son were also in the same boat. Between 4 and 5 a.m. the steamship 'England' came in sight, on which Terence hailed the ship, and asked if a pilot were wanted. Hearing there was sickness on board, he did not leave his boat. A bucket was lowered over the ship's side, and in it the pilot placed some official papers, showing that he was properly licensed. The documents were not returned until the next day. A 10-fathom rope was then thrown to him, by which the boat was towed astern at some considerable distance. These details I obtained during a conversation with Purcell. He told me the boat was towed as far as the quarantine ground between George's Island and the eastern shore, which would be a distance of about 12 miles. The 'England' anchored here for an hour or two, whilst the pilots went to Cunard's Wharf for further instructions how to act. On their return to the 'England' she was again got under weigh, the pilots now keeping their boat at a still greater distance astern. They took the ship to the west of MacNab's Island (about two miles further from Halifax), where she remained anchored in the main channel until she left for New York. Here all communication between Purcell, his son, and the 'England' ceased, for after seeing the steamer anchored for the second time, they went ashore in the boat with Terence. It will be better to complete the history of the Purcells before I again refer to the incidents connected with Terence. It is proved to a certainty by the corroborative testimony of Captain Grace and others, that neither of the Purcells was at any time on board the

'England.' Purcell returned home next morning (April 10th), to Portuguese Cove, 11 miles south of Halifax, and had an attack of diarrhœa on the following day (April 11th), which gradually got worse on the 12th, 13th, and 14th. By the 15th he was greatly prostrated, and then vomiting appeared for the first time. He was always free from cramps. Two of his children (aged 5½ and 3 years) were seized on the 15th with slight symptoms, with vomiting and debility, but quickly recovered. On the 16th April, the eldest daughter, aged 15, was attacked. She was dangeously ill, with every symptom of true Asiatic cholera, and the attack was followed by reactionary fever of a low type. Thus, four individuals were attacked out of a family of nine persons, but there were no deaths. The type of the disease was probably greatly modified by the fair sanitary condition of the house and immediate locality. I found Purcell's house to be in an airy situation, on elevated ground, that is, at least, 50 feet above the sea level. It was open to all winds. During the epidemic all the windows were kept open; the rooms were of fair size, though not lofty.

"I must now return to the history of the other pilot Terence. He left the anchorage ground of the steamship 'England' on the 9th April in the same boat as the two Purcells, and went ashore. Next day (10th April) he was employed to pilot the block ship 'Pyramus' from near the dockyard to the steamship 'England,' as the block ship was about to be made use of as a hospital for the cholera cases. He then returned to Halifax without going on board the 'England,' as he himself affirmed, and Captain Grace, who commanded the steamship, also bears out the statement. I have, in addition the evidence of the Rev. J. Carmody, that Terence on his death-bed declared he had never at any time been on board the 'England.' Terence slept that night (10th April), or rather, went to bed at a boarding house in Water Street, Halifax. While in bed he was seized with vomiting, cramps, and purging, and next morning (April 11th), got in a boat and was rowed home to Portuguese Cove (where Purcell also lived), a small fishing settlement, about 11 miles distant by sea, to the south of Halifax. In his (Terence's) case there was much collapse, but it was followed by reaction and low fever, from which he died on the 19th April, after an illness of nine days' duration.

"On the 14th April, or three days after Terence returned to his home, his daughter Elizabeth, aged five years, was seized with acute cholera at 6 a.m., and died the same evening at 9 o'clock. Next day (15th) three children were prostrated. Mary, aged three years, who slept with her father, had a severe attack, and died on the 17th, all the symptoms of Asiatic cholera having been present. Catherine, aged nine years, was dangerously ill; she recovered after consecutive fever. Susan, a year old, at one time seemed almost at the point of death, but reaction took place, and she recovered.

"Out of five children living at home, only one (a boy aged eight years) escaped an attack. He slept in a room by himself, and was out of doors all day. Mrs. Terence, to the great surprise of herself, escaped. She declared she was frequently covered with the cholera discharges from the children. When I inspected her cottage it did not appear astonishing to me that the disease should have shown more malignancy than in the house of the man Purcell. Terence's cottage was on the lowest level of the village, pretty close to the sea. The land sloped upwards, very near the back of the house, and in wet weather the surface water ran, or found its way under the flooring, where it was more or less dammed up. The rooms were small, with low ceilings, and badly ventilated.

"Nine cases appeared among the two families of greater or less severity. Two of them were so slight, that they could scarcely be called cholera; but it will be interesting to determine the probable period of incubation of the disease. I find one person suffered on the second day after exposure to contagion, two on the third day, three on the fourth, two on the fifth, and one on the sixth. The two piliots contracted the disease, strictly speaking, by means of infection, one 40 hours after exposure, the other, 52 hours after.

"No other cases appeared at Portuguese Cove, nor, in fact, anywhere in the province, with the exception of several in a family residing at Freshwater, the history of which is as follows:—

"A man named Evans, a puddler, in very indigent circumstances, his wife and two children, were living in a small cottage, not by any means in a good sanitary state, near the sea at Freshwater, which part of the town forms the

southern suburb of Halifax. A large quantity of bedding, saturated with cholera discharges, had been thrown overboard from the steamship 'England' soon after her arrival, and for many days allowed to float about the harbour. Some of it drifted ashore at Freshwater, close to Evans' abode, and a woman living in the same house declared that she had seen his children playing with it. Dr. Woodill, who afterwards attended the family, told me that Evans also stated to him that his two children had picked up and had been playing with some of the floating bedding. There is at the same time a strong suspicion that several of the family had been sleeping on an infected mattress. It is quite certain that some bedding had drifted ashore at that spot, and that Evans' children were playing close about it.

"On the 22nd April, his eldest child, a girl about two years old was seized with cholera, after having had diarrhœa for nearly a week. She was conveyed to the city hospital, and died next day. The entire family was then sent to the hospital, and kept in a state of isolation. On the 24th, two days after the seizure of the eldest child, the second, a girl aged 13 months, was prostrated. Her case was a very severe one, but she recovered. Next, the mother, aged 35, was seized on the 25th, and appeared to die from exhaustion on the 30th. No consecutive fever was apparent, but Dr. Woodill informed me that a day or two before death gangrene of the nose made its appearance. No post-mortem examination was made in either of the fatal cases. The father had diarrhœa throughout, but declared he was at all times subject to it.

"I was very anxious to find the man Evans, in order to cross-examine him as to whether any of the family did actually sleep on the infected bedding, but after being released from quarantine Evans was lost sight of, and could not be found. His house had been pulled down while the whole family were in the city hospital. The situation of the house was decidedly bad; it was close to the bridge at Freshwater, at the point where the small stream runs into the sea, and there was an extensive surface of soft, black, offensive mud in the immediate vicinity.

"The evidence of the propagation of cholera by means of fomites is exceedingly strong in the Freshwater case, although, perhaps, not quite conclusive. There were no other cases in Freshwater or in Halifax."*

The Diffusion in New York, 1866.

These slight infections of the continent of America, on the coast of Nova Scotia, do not appear to have had any after consequences. But 13 days after the arrival of the "Virginia" in New York harbour, and 11 days after the arrival of the "England," cholera appeared in the city of New York, and from the 1st May, the date of the first case, to the week ending the 24th November caused 1,210 deaths.

In this appearance of cholera, as in the appearance in the State Emigrant Hospital in Ward's Island the previous year, the source of infection could not be traced. There was no likelihood of infection having been communicated either from the "Virginia" or the "England." These ships, their passengers and their crews, were then in strict quarantine in Lower Bay, and were not released from detention, the "Virginia," ship and crew, until the 21st May, passengers, the 3rd June; the "England," ship, crew, and passengers, the 10th May. Whence, then, came the infection if not from the cases of cholera brought into the port before the appearance of the disease in the city? To this Dr. Swinburne replies, "The answer is simple. Prior to the appearance of "cholera in the city, all persons exposed to the disease, either on the "passage or in this port, were detained during a period of 22 days, while "others, among whom there had been no appearance of cholera during "the voyage, but who came from European ports, where the disease is "known to have prevailed, were mingling with their friends in New York "in the course of from 10 to 14 days from the date of their probable "exposure to cholera."† In other words, while the quarantine arrange-

* *Statistical, Sanitary, and Medical Reports: Army Medical Department*, Vol. vi., pp. 365–367.

† *Report previously referred to* (p. 79), p. 40.

ments were efficient for the weeding out of obvious cases of cholera imported into the harbour, and so diminishing the quantity of infection liable to be brought into the city, they afforded little or no protection against the introduction of unmarked but not less mischievous forms of the malady. To such introduction the outbreak on Ward's Island in 1865, and the appearance of cholera in New York in May 1866, were to be attributed. In relation to this subject Dr. Elisha Harris observes of the first case of cholera in New York in 1866.* "How it chanced that an "industrious and temperate housewife (Mrs. Jenkins), residing on the "hill-top that overlooks the southern end of Ward's Island, becomes the "first victim may never be explained so as not to admit just doubts of its "exotic origin. Yet this should be stated, namely, that there were as "strong probabilities that the grounds and privy pertaining to that "tenant house (of which she was mistress) would be contaminated by "recently-landed emigrants † as that the lodging-houses in the lower "wards would become infected. Again, in the beginning of the "previous winter, 27 persons with cholera died and were buried on "Ward's Island, within one mile from the spot where Mrs. Jenkins "died." He observes, moreover, in regard to the topographical distribution of the first 25 fatal cases of cholera in the city: "Every one "resided in, or frequented, localities that were daily traversed by "freshly-landed immigrants. This fact must not be regarded as establishing any dependence of the cholera upon such near presence of "immigrants, their foul beds and clothing, or their choleraic diarrhœas, "for, notwithstanding the fact that these good and sufficient causes of "infection were both suspected and fully anticipated, nothing has been, "or is ever likely to be, positively known regarding their relation "to outbreaks of cholera in New York. The city is too densely "crowded and the mixing of the population is too promiscuous and "utterly unnoticed and unregistered to warrant any attempt to "trace the connexion of events and acts that may have occurred daily in "the places where the cholera poison was received into the system."‡

I do not propose to follow the further course of cholera during the

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* *Report of the Metropolitan Board of Health, New York*, 1866. Epidemic Cholera in the Metropolitan Sanitary Districts during the year 1866, p. 168 and 187.

† Writing of the early investigation of this case, and on the particular privy referred to, Dr. Elisha Harris says:—"All that was seen and all the testimony then obtained conduced to the opinion that Mrs. Jenkins died of cholera, but that possibly it might have been produced by the septic effluvia of a mass of privy manure which some weeks previously had been mixed with soil and garbage refuse; and during the week previous to her illness, had, under her superintendence, and partly by her own hands, been spread upon her garden. Indeed, it was then, and is still, deemed highly probable that the cause of that sudden and fatal illness was somehow connected with that mass of privy soil which was the accumulation from that tenant population and trampers of the open area about them the previous four months. But the evidence simply amounted to this, that Mrs. J., as mistress of the premises, had, by her personal superintendence of the distribution of that manure, been more frequently exposed to its effluvium than any other one of the 35 inhabitants of her house, and that, as they had all used a new privy several weeks, there was no reason to suppose that any one except Mrs. J. and her hired man had been directly exposed to the old privy pit" (p. 167.)

‡ During the period immediately preceding, and the continuance of, the epidemic in New York, more than 50,000 emigrants from countries on the continent of Europe in which cholera was present at the time of their emigration, were landed at the Castle Garden emigrant depôt in New York (*Report of Metropolitan Board of Health, New York*, 1866, p. 18). The total number of ships which came into the harbour having cholera on board or in the course of their voyage, during this time, was 18. These ships brought 8,501 passengers, and their crews numbered 965. There had been on board them 495 deaths from cholera at sea, and while the passengers and crews were detained in quarantine there were among them 608 cases of cholera, of which 242 died. (Dr. Swinburne's *Report*, p. 71).

diffusion of 1866, and subsequent years on the continent of America. My present purpose is limited to describing the facts relating to the communication of the disease from the Old World to the New World in 1865 and 1866.

4.—*The Diffusion to North Western Africa and to West Africa.*

North-West and West Africa, 1865-69.

Algeria, 1865-1867.

West of Egypt cholera, so far as is known, appeared first in this diffusion in Algiers. Here, on the 4th September, 1865, a soldier of the 3rd African battalion, nine days after he had left Marseille, where he had staid several days on his way from Paris to Algeria, and where cholera was then prevalent as well as in Paris, was seized with well-marked cholera. Nine days after the occurrence of this case two of a detatchment of hospital attendants, in number 262, and recently landed from Marseille,* were sent into the Dey hospital suffering from cholera. Five other cases were received into the hospital on the 15th, and others in quick succession up to a total number of 15. On the 17th September two patients in the same division of the hospital where the cases of cholera were treated were attacked with the disease, and from this date cholera spread in the wards until not less than 69 patients and attendants had been attacked before the close of the month. During the same period, in addition to the 15 cases from the detachment of hospital attendants, but seven other cases had been received into the hospital, soldiers whose relation to previous seizures was not determined, but some of whom had probably been on duty in the hospital guard. On the 26th September, the wife of a military-bed maker, living in a house adjoining the quarters occupied by the detachment of hospital attendants, when cholera appeared among them, was attacked with fatal cholera. This was the first case among the civil population. The disease now began to extend both among the civil population and the garrison, and it continued in the city for four months.

I have not been able to find any account of the probable loss of life from cholera in Algiers during this outbreak. The disease appears to have been general in the city, and it probably extended thence to the neighbouring province. It is not, however, until 1867 that I have information as to the further progress of cholera in Algeria. In that year the disease was present in every province of the country, and it is reported to have been very fatal among the Arab tribes. At the close of October it had ceased in the province of Algiers, but it was still prevalent, although decreasing, in the provinces of Oran and Constantine. The last-named province had been re-infected at several places on the sea-coast and on its eastern frontier, from Tunis, towards the close of July or at the beginning of August; and there can be little doubt that cholera was transmitted from the province of Oran to Morocco during the year. It is greatly to be regretted that no official account of the prevalence of cholera in Algeria during the years 1865, 1866, and 1867 should have been published.†

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* I take the facts relating to this appearance of cholera in Algiers from the work of Drs. Vincent and Collardot, *Le Choléra d'après les neuf Épidémies qui ont régne à Alger depuis* 1835, *jusqu'en* 1865. (Paris, 1867.) The date of arrival of the detachment of hospital attendants in Algiers is not stated, but it is said that the disease appeared among the men after an incubation of from 15 to 20 days. In calculating the probable period of incubation of the case received into the hospital on the 4th September, Drs. Vincent and Collardot include eight days stay at Marseille, making the period in this case 17 days.

† It was stated in some of the French medical journals at the close of 1867, but without the source of information being given, that the loss of life from cholera in Algeria that year was estimated at 80,000.

Early in 1867 cholera appeared in the Regency of Tunis at a time of dearth. The disease was first certainly noted on an estate called Enseir Zeriba, near the city of Tunis, where a contraband trade was known to be maintained with Sicily; and it was supposed to have been imported from that island where cholera had been introduced the previous year, and where it prevailed with pestilential severity in the year under consideration. But as all quarantine restrictions upon shipping had been removed since the summer of 1866, and Tunis was in free communication with other places which were afterwards known to be infected, it was impossible to discover the actual source of the infection, or, indeed, to say when it may have been introduced into the Regency.

Tunis, 1867.

Cholera was probably present in the city of Tunis in March, and in April there was no longer question of its existence there. A sharp outbreak of the disease appears to have occurred at the beginning of April, extending into May, and then seemingly coming to an end for a short time. The malady reappeared a little later, and assumed formidable proportions in July. The deaths during the latter month were, it is believed, from 300 to 400 daily.

In May, two bodies of troops left the city, one for the northern, the other for the southern districts of the Regency, to collect the annual impost. These troops carried the disease with them, and suffering considerable losses from it themselves, infected the various towns and districts they visited. Thus, in the northern districts, Bizerta, Beja, Keff, and the neighbouring districts were in succession infected; and in the southern districts Susa and Sfax, and the towns in the Jerid (Belad-el-Jerid, "the country of date palms"). In the sea port towns and other of the larger centres of population the disease was very severe, and the dissemination in the track of the troops, and from the different centres of infection set up by them, appears to have been general. Towards the close of July, or at the beginning of August, cholera had reached and passed the Algerian frontier at two points, one on the limits of the Sahara region in the Jerid, where little could be known of the further movements of the disease; the other in the district of Keff, by which route it reached Biskra, in the province of Constantine. On the sea-coast, moreover, it was transmitted from Tunisian ports to Bona and Phillipville, in the same province.*

Morocco, 1868.

While this infection of Algeria from Tunis was in progress on the eastern frontier, cholera being already widely prevalent in that country, it is highly probable that across the western frontier the disease was spreading into Morocco. There does not seem, however, to be any definite information of the prevalence of the disease in the latter country until its appearance in Tangiers at the beginning of February, 1868, and its subsequent occurrence in all the important seaport towns on the Atlantic coast. From the time of its appearance in Tangiers to the date of the latest information regarding it, early in August, the disease seems to have been prevalent along the whole coast-line of Morocco, and in the districts adjacent. Of the districts east of Tangiers it is only known that Tetuan and the towns of that district were reported free from cholera at the close of July or commencement of August. Of the districts west of Tangiers it is known that the disease appeared on the coast at Arzilla, El Araish (Larache), Sallee, Robat, Dar el Beida, Mazagan, Saffi, and Mogador. In the district of Mogador the

* *Intorno al Cholera di Tunisi dell' anno* 1867, per Dottor Giovanni Ferrini; Milano, 1868.

disease continued until late in October. This general infection of the seaport towns of Morocco, does not appear to have been, except to a limited extent, a dissemination from port to port. So far as the meagre facts relating to the distribution of the disease admit of an interpretation, they would seem to indicate a propagation of the disease to the coast from the interior, and in continuation of the diffusion of cholera in the province of Oran (Algeria) the previous year.

In some sort tending to confirm this inference, as indicating the presence of cholera in a very active form in the remoter districts of Morocco about the middle of 1868, and of which no knowledge reached Her Majesty's representatives on the coast at the time, is the remarkable fact I have now to relate of the transmission of cholera from Morocco across the Sahara to Senegambia.

Senegambia, 1868-69.

Early in November cholera, until that time, so far as my present information extends, unknown in Senegambia, broke out at Podor, on the River Senegal, following upon the arrival of a caravan from Morocco. Podor is a large town situated 150 miles from the sea coast, or thereabouts, and is the principal centre of the considerable trade carried on between the native towns on the Senegal and Morocco, with which country it maintains constant communications by land.* From Podor the disease spread both up and down the river. Of its upward progress nothing is known but the fact. In its downward progress cholera was observed first at the mouth of the river, at St. Louis, and afterwards at Richard Toll and Dagana, lying on the stream between Podor and St. Louis. At Saint Louis the disease appeared towards the close of November, and from the 1st to the 15th December, there were at least 1,800 deaths among a population of 12,000.

At the time of the outbreak in Saint Louis, there were many natives there from the Joloff country, lying between the rivers Senegal and Gambia, and Mandingoes from the Upper Gambia, the latter having fled to St. Louis in consequence of an attack upon their tribe by a neighbouring tribe. When cholera broke out in St. Louis, these natives fled into the Joloff country, carrying with them the disease and communicating it to the numerous populous villages which exist in the western portion. Here it was propagated from village to village, being heard of at Nyanee, on the border of the Mandingoe country, in February 1869.

On the 10th March 1869 cholera appeared in MacCarthy's Island, on the River Gambia, at the beginning of the ground nut season, when the natives were flocking to it from the mainland, for work in the ground nut harvest. MacCarthy's Island is situated 180 miles from Bathurst, up the river, and has an ordinary population of from 300 to 400, under the supervision of an English agent, of whom 80 died of the disease. On the appearance of cholera in the island, the native labourers from the mainland, and many families, fled, some up stream and some down stream. By the fugitives up stream the disease was carried into the Bondou country lying between the upper waters of the Gambia and the Senegal; by the fugitives down stream it was carried to Doomasangsang, a trading

* When the appearance of cholera in Senegambia, at Podor first became known in England, I had an opportunity of conversing with the late Mr. Winwood Reade on the subject. Mr. Reade had shortly before visited Podor. He told me that from what he had himself observed of the relations maintained between Podor and Morocco, and what he had learned of the caravan routes commonly followed across the Sahara to the Senegal, he saw no improbability in the transmission of the disease by caravans, and the infection of the villages on the routes. The Sahara is, in fact, much more populous in the part of it traversed by these routes than is commonly understood.

station, 100 miles below MacCarthy's Island, which it nearly depopulated. From Doomasangsang cholera was propagated to Bathurst where the first case was observed on the 4th May 1869, in the person of a negro woman who had arrived a few hours before from Doomasangsang. Other cases may have occurred in Bathurst before, as several dead bodies of negroes had been found in the streets about this time, the cause of whose death was not in the first instance determined, and who had very probably been landed ill in the night from canoes coming from up-stream. When later the Coroner directed a post-mortem examination of a corpse thus discovered, and having no external marks of injury, the intestines were found filled with the "rice-water" discharge characteristic of cholera. In Bathurst, during the months of May and June 1869 among a population (civil) numbering at the beginning of the outbreak 4,250 there were 1,174 deaths from cholera registered; 12 deaths occurring among the troops (coloured, 101 strong), 3 among their families, and 2 among the European residents.

Senegambia, 1868-69.

After the appearance of cholera at Bathurst, the disease broke out at Albreda, a trading station nineteen miles up the Gambia, which to that time had escaped; and on the coast at Dakar, Cape de Verde peninsula, about midway between Bathurst and St. Louis. In both these instances the disease is stated to have been transmitted from Bathurst. From Dakar cholera passed to the neighbouring town of Rufisque, and from Rufisque to the adjacent island and town of Goree, where the disease appeared in June.

Bulama and the Rio Grande, 1869.

South of Bathurst cholera was next heard of, in September, at Cacheo (at the mouth of the river of that name), at Bulama, the easternmost of the Bissagos islands (where there were 30 deaths from the 10th September to the 18th October), at Bissao and other places on the adjacent mainland, at the mouth of the Rio Grande, and finally on the banks of that river, where, at the time of the latest news received of its progress (October 1869), the disease was making its way into the interior.

In this the first reputed extension of cholera in West Africa, the disease does not appear to have been disseminated lower south than the Rio Grande. (*See* Maps II.–VI.)

5.—*The Diffusion in Egypt, Nubia, and East Africa.*

Egypt, Nubia, and Eastern Africa, 1865-71.

Egypt, 1865.

I have in preceding sections described the diffusion of cholera from Alexandria, as the starting point, in 1865, northwards to Europe, and the secondary diffusions from Europe the same year, eastwards to parts of Asia Minor and Caucasia, westwards to the continent of America, and southwards to North Africa, west of the original starting point. I have further described as briefly as is consistent with such clearness as the facts in my possession admit of, the succession of events following upon the original diffusion, except in the western hemisphere, so as to show their relationship to that diffusion. I now, having completed the account of the diffusion northwards and westwards as far as I had proposed, return to the starting point of the diffusion in Lower Egypt, and proceed to a description of the other lines of diffusion followed by the disease, also in 1865, contemporaneously with the diffusion northwards and westwards. While cholera was being disseminated from Alexandria on the northern and western coasts of the Mediterranean, it was also being disseminated on the eastern coast, whence through Syria it passed into Mesopotamia. Moreover, at the same time, the disease was spreading from more than one point throughout Lower Egypt, and travelling along the valley of the Nile directly southwards, beginning

in all likelihood a journey either there, or, as will be seen, more probably from Suakin, of which the end was not reached six years afterwards, when the malady having extended through East Africa to Quilimane, in Mozambique, was last heard of spreading into the interior of South Africa.

And first of this southern diffusion, and the prevalence of the disease in Egypt.

Egypt, 1865.

On the 21st May 1865, the captain of the ship which brought the first detachment of pilgrims returning from the Hejaz by way of Suez, and his wife, were attacked with cholera in Suez, the second day after the arrival of the ship there (19th May). The next day (the 22nd May) a case of cholera was observed at Damanhur, on the line of railway from Suez to Alexandria, among a body of pilgrims who had come from the former port. On the 2nd June, a case of cholera occurred among the inhabitants of Alexandria who were in communication with the pilgrims having other destinations, and who were waiting for embarkation; and on the 11th June, the existence of cholera in the city was officially recognized. On the 17th June, the disease appeared at Cairo, first at the railway station among persons coming from Suez. In no previous epidemic had cholera manifested itself in Alexandria before Cairo. An explanation of this difference is to be sought in the changed conditions of transit between the two cities and Suez since the epidemic of 1855. By the establishment of railway communication in the interval, it became possible to hasten the passage through Egypt to Alexandria of those pilgrims who simply traversed the country for other destinations in the basin of the Mediterranean. This was effected by trains specially detailed for the purpose, and thus the chances of infection of Alexandria were indefinitely multiplied as compared with Cairo and other intermediate towns.

From the several points mentioned, and others, cholera spread over Lower Egypt, and prevailed there until the month of September. During this period the total ascertained deaths in this division of the country numbered 43,287.

In Middle Egypt the disease appeared in the province of Minieh on the 30th of June 1865, and during a prevalence of three months or thereabouts, it caused in the three provinces of this division of the country 3,846 deaths.

Upper Egypt was invaded by cholera from the Hejaz by way of Kosseir about the same time as Lower Egypt; and it probably was also infected later from Middle Egypt along the Nile valley. In the province of Keneh the disease appeared on the 23rd July; the dates of appearance in the other provinces do not seem to have been ascertained. The total recorded mortality from cholera in Upper Egypt was 14,059, of which 713 occurred in the provinces of Kosseir and Esneh.

The population of Egypt on the 26th May 1865 was 4,841,677; the total reported mortality from cholera during the year was 61,192. (See *Appendix*, Table XXVI.)

Of the further movement of cholera up the Nile valley, beyond the frontier of Egypt, nothing is known; and of its prevalence in Nubia, but three isolated facts have come to light. These three facts, however, are of great importance in the history of the progress of the epidemic southwards. The first is the presence of cholera in Suakin in the month of June 1865; the second, the serious prevalence of cholera in Cassala, the capital of the province of Taka, from July to October 1865; the third, the presence of cholera in a grave form in the province of Taka in March 1866.

ubia, 1865.

The fact of the prevalence of cholera at Cassala in July–October 1865, was ascertained by Mr. Rassam, when he passed through Cassala, early

in November 1865, on his mission to Abyssinia.* Cassala is situated on the Abyssinian frontier, and is the principal military station of Egypt in Nubia. Its communications with Egypt are maintained through the port of Suakin, and the dates of prevalence of cholera in Cassala indicate that Suakin would be the starting point of the diffusion in this portion of the Khedive's dominions. The fact relating to the occurrence of cholera in the province of Taka in 1866, was reported to the Egyptian General Board of Health by H. E. Djaffer Pasha, the Governor General of Nubia.† He states that on the 29th March 1866, the Bedouins of the Beni-Amer Arab tribe, then encamped on the borders of a great lake, were surprised by a violent storm. One hundred men, women, and children were killed outright; and many animals, including six elephants and two hippopotamuses. The trees overlooking the lake were blasted, and the stones upon the banks appeared as if calcined. The next day cholera broke out in the tribe, and killed in a very short time ("en quelques moments") from 500 to 600 persons, the disease disappearing as suddenly as it appeared.

Abyssinia, 1865-1866.

Early in October cholera appeared in the town and island of Massowah, on the Abyssinian coast, and extended to the adjoining district on the mainland. The disease had become very fatal when Mr. Rassam left Massowah on his Abyssinian mission on the 16th October.‡ Of the source of the outbreak there is no information, but it followed in succession upon the outbreak in Nubia, and was no doubt a continuation of the diffusion in that country along the districts bounding the Red Sea to the south. Mr. Rassam, in the narrative of his mission, furnishes incidentally the explanation of the escape of Massowah from the primary diffusion of cholera from the Hejaz in 1865. Under date the 2nd June 1865, Mr. Rassam being then at Massowah, he notes:—

"News arrived that no less than 15 out of 30 persons who had gone to "Mecca from Massowah had been carried off by cholera, which had "broken out among the Hajj."§ It would appear then that the number of pilgrims who visited Mecca from Massowah in the pilgrimage of that year was small; and as the principal thoroughfare for Mahommedan pilgrims from Abyssinia and Eastern Nigritia is by way of the port of Suakin, the liability of Massowah to infection would be considerably less than the liability of the first-named port, and of Kosseir.‖

Of the subsequent progress of cholera in Abyssinia, there is only such knowledge as was acquired by the Abyssinian captives, and Mr. Rassam's mission, one of the members of which was Dr. Blanc.

During the stay of the mission, first as visitors, afterwards as captives, at Zagé, on the southern shore of Lake Tzana, March–April 1866, Dr. Blanc learned that cholera had been "making havoc" in Tigré, the district lying between the coast of the Red Sea, at Massowah, and Central Abyssinia, where the mission then was, and that the disease had

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* *Further Correspondence respecting the British Captives in Abyssinia.* Presented to Parliament, August 10th, 1866, p. 6. Mr. Rassam to Lieut.-Col. Merewether, Metemah, 27th November 1865.

† Procès-Verbaux, 1865–66, p. 212.

‡ Narrative of the British Mission to Theodore, King of Abyssinia, vol. I., ch. IV.

§ Narrative, vol. I., p. 78.

‖ I have no means of knowing the actual number of pilgrims and other passengers travelling by way of Massowah to Jidda in 1865; but, in 1866, from the 18th March to the 2nd June, 12 ships entered Jidda harbour from Massowah, carrying 147 passengers, and in addition an Ottoman frigate with 415 soldiers. During the same period there arrived at Jidda from Suakin 37 ships, carrying 1,613 passengers, and from Kosseir 13 ships, carrying 1,123 passengers.

Abyssinia, 1865-66.

extended to other districts.* This prevalence in Tigré and extension towards the interior was clearly a continuation of the outbreak which the mission had witnessed on the coast at Massowah in the previous year, and probably also of direct infection propagated across the Nubian frontier. The members of the mission, therefore, with this knowledge of a previous southward diffusion of cholera in the northern districts of Abyssinia, were not surprised when, at the end of May 1866,† cholera appeared at King Theodore's camp at Zagé, and subsequently became prevalent on the south-eastern shore of the lake, and in the district intervening between the lake and Debra Tabor to the east. The disease continued in the King's camp for "several weeks,"‡ and was especially fatal when the camp, in June, was fixed at Kourata, on the eastern shore of the lake.§ The captives and the camp were at Gaffat in July, and cholera broke out there in that month.

Nothing is known of the progress of cholera south of Lake Tzana, or in other localities than those occupied by King Theodore's camp at the time in question. The epidemic then manifested no abatement of diffusiveness, and it is to be inferred that the populations south of Lake Tzana would suffer from it equally with those to the north. Positive knowledge ceases with the information derived from the captives.

East Africa, 1869-71.

From the period when cholera was prevalent on the borders of Lake Tzana in 1866 to the year 1869, cholera was not heard of in East Africa.

In October 1869, towards the close of the month, it was rumoured in Zanzibar that caravans trading from that island in the districts beyond the Wamasai, on the mainland, had been attacked with a deadly

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* *The Story of the Captives.* A Narrative of the Events of Mr. Rassam's Mission to Abyssinia. By Dr. Blanc, one of the captives, 1868, p. 65.

† Mr, Rassam, "Narrative," vol. ii., p. 123.

‡ *Story of the Captives*, p. 67.

§ "On the 6th of June, his Majesty [King Theodore] left Zagay with his army; Mr. Rassam and the other prisoners accompanied him, all the heavy baggage had been sent by boat to Kourata. On the 9th, his Majesty encamped on a low promontory south of Kourata. Cholera had by this time broken out in the camp, and hundreds were dying daily. In the hope of improving the sanitary condition of the army the Emperor moved his camp to some high ground, a mile or so north of the town, but the epidemic continued to rage with great virulence, both in the camp and in the town. The church was so completely choked up with dead bodies that no more could be admitted, and the adjoining streets offered the sad sight of countless corpses surrounded by their sorrowful relatives, awaiting for days and nights the hallowed grave in the now crowded cemetery. Small-pox and typhus fever also made their appearance, and claimed the victims cholera had spared. On the 12th June we received orders to join the camp, as his Majesty intended to leave on the following day for the higher and more healthy province of Begemder. On the 13th, at early morning, the camp was struck, and we encamped in the evening on the banks of the Gumara, a tributary of the Nile. The next day the march was resumed. We had been more or less amending since our departure from Kourata and Outva (a beautiful plateau). Our halting place of the 14th must have been several thousand feet higher than the lake, nevertheless, cholera, small-pox, and typhus fever continued unabated. His Majesty inquired what was usually done in our country under similar circumstances. We advised him to proceed at once to the higher plateau of Begemder, to leave his sick on the side of Debra Tabor, and to break up as far as possible his army, and distribute it over the whole province, selecting a few healthy and isolated localities where every fresh case that broke out should be sent. His Majesty acted upon this advice, and before long had the satisfaction of seeing the several epidemics lose their virulence, and before several weeks, disappear altogether."—Dr. Blanc, "*Story of the Captives*," pp. 66–67.

"[*Kourata.*] . . . The 9th June [1866], the King sent to say that about one thousand of his soldiers and camp followers had been attacked during the night by cholera, of whom about 300 had died already."—Mr. Rassam, *Narrative*, vol. ii., p. 128.

disease. This disease was stated to be then fatally prevalent in the Usambara country, and to have made its way to the coast towns of Tanga and Pangani, coming from the interior. The news was speedily confirmed, and any doubt which might have existed as to the nature of the malady was dissipated by the appearance of cholera, on the 27th October 1869, if not a few days earlier, in Zanzibar, believed to have been imported from Pangani, with which port the island was in daily communication.

The Wamasai occupy a district lying midway between the Victoria Nyanza lake and the sea coast, beyond the first great range of mountains, of which Kilimanjaro is chief. The Usambara country lies near to the coast in rear of the Wadigo district, which has a coast-line extending from the town and port of Tanga on the north, to the town and port of Pangani on the south. Beyond the Wamasai country, east to the position of the Victoria Nyanza, and north into the Gallas country, south of Abyssinia, our knowledge of localities is imperfect, and rests upon information derived from the leaders of caravans. Dr. Christie has made the source of the cholera which appeared in East Africa in 1869 a subject of particular investigation, and his researches leave no doubt that the disease came from the interior to the sea coast, opposite Pemba Island. The following is the account he gives of the result of his inquiries at the time:—

"The country occupied by the Wamasai lies to the west of Usambara, and is represented in the maps of Africa by a blank. Little is known of the people themselves and still less of their country, as it has never been visited by Europeans, and we depend for our information regarding them on passers through the country, the boundaries to the north, south, and west being entirely unknown. The Wamasai are a pastoral people; they have no villages and move about from one district to another, according to the season, to find pasturage for their flocks. In manners and customs, and probably in origin also, they are closely allied to the Mavite who inhabit the country to the north-west of Lake Nyassa. They are represented as being an exceedingly fierce and warlike tribe, the terror of all their neighbours, and during times of scarcity they make raids on the coast towns, devastating the country in their line of march, and carrying with them all the cattle. A few years ago they harried the country between their own territory and Mombassa, and even threatened the town. To say that the Wamasai are out is sufficient to strike terror to the hearts of all their neighbours and make them fly from their line of march.

"Pangani and Tanga are situated a little to the north of the island of Zanzibar, and are the starting points for caravans proceeding to the interior towards the Victoria N'Yanza and further to the north. These caravans skirt the Usambara country in their course, and pass through the territory of the Wamasai, the larger caravans paying the usual black-mail levied, and the smaller exchanging commodities and then returning to the coast towns.* . . . . "I had an opportunity of examining lately two men who were leaders of the caravan which penetrated the Masai country, and brought to the coast the first intelligence of the existence of the epidemic in the interior. Their narrative was one of great interest in many respects, and they seemed to be thoroughly acquainted with the territories described. One had made fifteen caravan journeys amongst the Masai and the other nine.

"The caravan left Pangani in November 1868, with over 1,000 men, and proceeded towards the interior, keeping the River Pangani, or Rufu, as it is called, higher up on the left. On the fourteenth day of marching they reached the Lake Jipe, and on the sixteenth day the town Urombo, near Mount Kilimanjaro, and on the twentieth Marago ya Kanga, the first Masai town. On the forty-ninth day, they reached the Masai encampment at Kisima in the the district of Laikepya, in the fifth month after their departure from the coast. There are many delays in travelling, and sometimes a caravan remains for more than a week in one place without moving. When at Kisima they were told that

* *Transactions of the Epidemiological Society of London*, vol. iii., p. 268.

the Masai had made a raid on the Somali to the north, and that while in their country they were attacked with some deadly disease which they brought with them to their own country, but they had no name for it, and had never known it before. At Kisima the party which had reached the district separated in all directions to trade with the Masai, and, after being absent for about a month, they reunited and started on their return journey. One of their party died at Kisima, but they did not suspect it was cholera as it did not spread. On their return they made a detour, and kept Kilimanjaro to their left. On the seventh month they reached the town of Lytoketoke, not far from Kilimanjaro, and there they saw for the first time people dying of the plague or cholera. Formerly it was merely a matter of report, but when they saw those affected they knew at once the nature of the disease, and hastened towards the coast. Lytoketoke is six days from Harush, and when they reached that place they met a large caravan from Pangani going towards the Masai country. This caravan was told that the whole district was affected with cholera, and advised to return; but, not attending to this advice, the caravan pushed on, but altered their line, not passing in that of the returning caravan which reached the coast in safety, only one of their number having died. I have every reason to believe that the statement of these men is correct, as I had several opportunities of checking their distances. The town of Kisima must be considerably to the north of the equator. They said that they never went into the country of the Somali or Gallas, but that they had met traders from Brava who regularly trade in these districts. Their description of the countries through which they passed and the rivers crossed was of great interest, but foreign to the present inquiry.

"Another man, one who was with the caravan met on its inward journey, was examined previously, but not by myself personally. I regret this, as he was one of the few survivors who reached the coast, but I hope to be able hereafter to get hold of him.

"He stated that on the fifteenth day from Pangani, they arrived at Harush, where a portion remained to trade in the district; that the remainder passed on to Dasikera, where another portion remained, and that, as ivory was very dear and scarce, the remainder pushed on to the district of Laikepya, where the great body of the Masai were. When there, they knew that the Masai were dying in great numbers, and as those of the expedition were also attacked, they collected their ivory and goods, and, having concealed the greater part in a hole which they dug, fled to the coast. On their return they passed through the districts of Dasikera and Harush, but the whole of the trading party in these two places died. After their arrival at the coast cholera appeared, and it appeared also in all the districts through which they passed. Out of about 150 of the party that started from the frontier of the Masai district only seven reached the coast alive.

"This man stated that when in Laikepya he heard that the Masai had made an attack on the Soma-Gurra tribe, who possess camels, horses, and cattle, and that they had brought the disease to their own country. He also said that the next tribe to the Soma-Gurra was the Galla Borani, whose territory is on the south of the Jub river. This brings us very near to the line of the cholera epidemic of 1865, stretching from Berbera to Gananah and Barderah, but beyond the district of the Soma-Gurra I have not been able to trace it. Investigations, however, from the direction of Brava have been set set on foot, as trading parties from that place visit Soma-Gurra, the distance being under a month. If the disease did not start from Berbera, it probably proceeded from Abyssinia, which is very likely; or from some place on the west coast, crossing at about Gondokoro. But conjecture is useless. I have requested several people about to start shortly for the Masai country to collect further information, both as to its origin and also regarding its devastations among the people."*

At the time when Dr. Christie wrote the foregoing paragraphs he was unaware of the prevalence of cholera in Central Abyssinia in the summer of 1866, and of the general movement of the disease from north to south in that country, along the route from Massowah to Enarea in the Galla country; and he had put aside, as incredible, a positive statement made by the Somalis, at the commencement of his investigations,

* Transactions of the Epidemiological Society, vol. 3, p. 283.

that the disease in the Masai country, and the district beyond, had come from Mecca through Abyssinia and the Galla country. Enarea, according to Mr. Plowden, is "the great emporium" of East Africa. This town "is frequented," he states, "by traders 'from Zanzibar and "Tajoora, from Massowah and Khartoom, from Darfoor and Khoor-"doofan, and it is said even from Darsala and Timbuctoo."* Direct communication is not maintained between Zanzibar and Enarea, but an indirect intercourse is kept up through the intermedium of the tribes on the borders of the Galla country, as the Soma-Gurra, and Galla Borani tribes referred to. Dr. Christie, with later information, has since examined, with special reference to the time occupied in the passage of caravans, and the difficulties they have to encounter in the route, the question of the possible transmission of cholera from Central Abyssinia in 1866, through the Galla country to the East Coast of Africa. As the result of an elaborate investigation he has come to the conclusion that, assuming the onward movement of cholera to have continued from Central Abyssinia, infecting the Galla country, and spreading along the different trade routes from Enarea, the disease could not have appeared on the East Coast earlier than 1869. In other words, he finds that the time of appearance of cholera on that coast, in that year, is consistent with the assumption that it was a continuation of the diffusion which, starting from Nubia in 1865—or more accurately from Mecca, by way of Suakin—had been last observed extending southwards in Central Abyssinia, in the summer of 1866; is consistent, in fact, with the statement of the Somalis.

That which happened with the caravans travelling eastwards to the coast from the Wamasai country in 1869, happened also with the caravans travelling westwards to Lake Tanganyika. Dr. Christie has ascertained that the same year the caravans returning from the Wamasai along the route to Unyanyembe and Ujiji, carried cholera along with them infecting the different stations through which they passed, including the towns mentioned. Along this route he has been able to trace the disease back as far as Tura and Kerewe, the former a halting station a little east of Unyanyembe, and the latter the place of meeting of the Arab traders who visit the regions to the south-east of the Victoria-Nyanza. He further shows that the different references to cholera this year (1869) in Dr. Livingstone's "Last Journals," indicate that the disease was propagated to Bambarre west of, and to Cazembe south of Lake Tanganyika; as also to the plateau of Labisa, west of Lake Nyassa.

As already stated cholera had appeared in Zanzibar at the close of October 1869. Here it spread throughout the town and island, and did not cease until the middle of July 1870. The visitation was terrible. It is estimated that the loss of life from the disease in the town was not less than 15,000, and throughout the island generally 25,000. Of the different races forming the population of the town and island, it is believed that there were destroyed by the pestilence $6\frac{1}{2}$ per cent. of the natives of India, 10 per cent. of the Arabs, and 25 per cent. of the negroes.†

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* *Correspondence respecting Abyssinia*, 1846–1848. Parliamentary Report, p. 7 and p. 112.

† "In 1835 Dr. Ruschenberger estimated the census of Zanzibar at 12,000 souls, "of whom two-thirds were slaves. In 1844 Dr. Krapf proposed 100,000 as the "population of the island, the greater number living in the capital. Captain "Guillain, in 1846, gave 20,000 to 25,000, slaves included. I assumed the "number, in 1857, as 25,000, which during the north-east monsoon, when a large "floating population flocks in, may rise to 40,000 and even to 45,000. The Consular "report for 1849 asserts it to be 'about 60,000.'"—Capt. R. F. Burton, *Zanzibar*, vol. I., p. 81.

I quote Dr. Christie's account of the further progress of the disease on the East African Coast:—

"On the arrival of the natives from the northern ports, I collected information regarding the spread of the epidemic to the north. It passed along the coast generally, attacking the inhabitants of all the towns in communication with Zanzibar. When direct communication with Lamoo was open on the change of the monsoon, the epidemic reappeared with greater violence than formerly when it first reached that place from Melinda. It lasted four months, and the only section of the population not attacked was the Indian. It also appeared at Mukdesha and Worsheikh, and affected the population of the maritime districts to a distance of from two to three or four days from the coast. It appears reasonable to suppose that it did not pass further inland in the districts to the north, simply because at that place the trade routes were closed, and the people residing in the several districts, belonging to distinct tribes, have no intercourse with their neighbours. The people from the inland tribes generally bring their produce to Brava, Merka, Mukdesha, and other places before the dhows leave for Zanzibar, and they return with their purchases at once. The produce that they bring consists of hides, ivory, and gums such as myrrh and arabic, but principally the two former; orchella weed and gum copal being a coast produce. The ivory and slave caravans starting from between Quiloa and the Pangani go at all seasons, and consequently those starting from infected districts carried the disease with them along their line of march. This epidemic reached to the north as far as the island of Socotra. The Socotra dhows leave Zanzibar very early, at the first break of the monsoon, and generally call at Mombassa, the whole passage being about 15 days. My Socotra friends state that in one of their dhows one man died on the passage, and that, on arrival at its destination, the disease broke out at Bunder Kadu, near to the principal town, Bunder Kalassia. It did not spread generally throughout the island, and there were only about 20 deaths at Bunder Kadu. They spoke of a former epidemic which was very fatal at Bunder Kalassia, and which I supposed to be that of 1858–59.

"The time has not yet arrived for the collection of full particulars regarding the spread of the epidemic to the south of Zanibar, so that the remarks to be made are incomplete, and some may require correction. The disease lingered in Mozambique and the neighbourhood for about eight months. On January 11th, 1871, it appeared at Ibo, to the north of Mozambique, and at about the same time at Quilimane to the south, being conveyed in both cases in dhows from the infected Mozambique district.

"My informant, the principal banyan merchant at Ibo, states positively that cholera did not reach that place by coast traffic, but by dhows. It lasted for a month and a half, and there were about 1,300 deaths, but no natives of India were attacked. Five of the higher class of Portuguese died, and 12 Portuguese soldiers. At the time of his departure from Ibo, about the beginning of May, no cases had occurred for about a month, the last case that he heard of being on the 11th of March, and he had heard that the epidemic had passed towards the interior to about five days' journey from the coast. The last case of cholera at Mozambique was in the month of March last.

"Native merchants from Nosi-bé inform me that cholera appeared at Majunga, on the north-west coast of Madagascar, in August 1870, and that it was conveyed in native craft from Mozambique. It was communicated from Majunga to the French island, Nossi-bé, in September. The disease was there confined to the native town, Ambanourou, around which a *cordon militaire* was placed. The epidemic did not spread at the time. During this epidemic there were about 160 deaths. In March 1871 cholera again appeared at Nossi-bé at the time of the arrival of the Seychelles mail, and three men on board the mail steamer died. I have heard nothing regarding the mode of communication. The disease was confined entirely to the French town of Helleville; not many deaths had occurred, and a cordon was placed round the town.

"In December 1870 a quarantine of 14 days, afterwards of 21 days, was established at Mauritius, as the north coast of Madagascar was infected, and as cases, supposed to be sporadic, had occurred in Mauritius. In January 1871 it is reported from the same island that several cases had occurred, usually fatal, and fearing that the malady had been conveyed from Madagascar, a petition had been presented to Government, praying that communication between Mada-

gascar and Mauritius may be 'entirely prohibited' until the latter island may be free of cholera."* (*See* Appendix, Note D.)

For detailed information as to the progress of this epidemic in East Africa I would refer to Dr. Christie's forthcoming work. His account of the early origin and progress of the epidemic is a unique example of the application of geographical research in the elucidation of an etiological question.

Not to interrupt the continuous history of the diffusion of cholera southwards in East Africa from 1865 to 1871, I have, for the moment, left unnoticed a reappearance of cholera in the Hejaz and Lower Egypt in 1866.

Egypt, 1866.

Early in the year there were some indications that the outbreak of 1865 had not wholly come to an end with the close of that year. On the 8th March 1866, an Italian workman, who had recently come from Chalouf, on the Isthmus of Suez, died in the European Hospital, Alexandria, of cholera, certified to be "Asiatic cholera," by a commission of the General Board of Health. A commission of the Board was also sent to Chalouf, to investigate the state of things there. No cholera was found in that place, but a fatal form of diarrhœa; and the commission recommended the closure of the workshops of the Isthmus Canal Company, at Chalouf, for a period. On the 23rd of March a death from cholera occurred on board the ship "Trent," in the harbour of Alexandria; on the 28th a case of cholera was admitted into the Deaconesses Hospital, in the same city; and on the 27th–28th a case occurred in Suez. These three cases were regarded as sporadic. Three so-called sporadic cases were also reported to the General Board of Health in April. One of these occurred in Alexandria on the 3rd of April, one on the 17th (a fatal case on board the French steamer "Mœris," in the harbour), and the third (also a fatal case), on the 26th April at Suez. Diarrhœa still continued during this month in Chalouf. At the close of May the attention of the Board was arrested by an unusual mortality reported from Suez. The deaths ordinarily occurring in that town, during this month, numbered on the average from 14 to 16. But at the meeting of the Board on the 30th, not less than 33 were reported; and among these three rapidly fatal cases occurring respectively on the 26th, 27th, and 28th of the month, of a choleraic disease, designated by the Board's sanitary agent at Suez, Dr. Anton Flora, as "*fièvre pernicieuse, choléri*form*e.*"† Four other fatal cases of this disease were reported by

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* *Transactions of the Epidemiological Society of London.* Vol. 3, p. 285.

† The following is extracted from Dr. Flora's Reports to the Egyptian General Board of Health at the time. (Procès-Verbaux, 1865–66, pp. 146–147) :—

Suez, 26e Mai 1866.—"(1 heure après-midi.)—Aujourd'hui 26 Mai, vers une heure de l'après-midi on m'a appelé pour me rendre auprès d'une blanchisseuse Syrienne qu'on m'a dit avoir été subitément saisie d'un froid extrême.

"J'ai trouvé une femme de quarante-cinq à cinquante ans; les yeux étaient enfoncés très-profondément dans les orbites, les joues avaient pris une couleur jaunâtre et étaient contractées, les lèvres, la langue, les bras, les jambes étaient froids. Le ventre était contracté.

"Il y avait des vomissements aussitôt qu'on faisait avaler quelque boisson à la malade.

"Le pouls était extrêmement faible, mais néanmoins d'une fréquence normale.

"Il existait des douleurs très-fortes aux reins et au ventre, telles que la malade poussait des plaintes continuelles. Ma première impression a été qu'il s'agissait de douleurs rhumatismales. [In a subsequent description of this case (*see* below) taken from his note-book, Dr. Flora states that his first impression was that the disease was cholera.]

"3 heures.—La malade devient de plus en plus froide. Le pouls n'est presque

Dr. Flora before the 5th of June, and a fifth case occurred on that day. On the 30th May a case of cholera occurred in Alexandria, which ended fatally on the 2nd June; and on the 9th a doubtful case occurred in Suez. On the 7th July a fatal case of cholera occurred in Suez, and on the 8th and 11th, 4 cases, 2 fatal, in Alexandria. At the beginning of August "cholerine" was reported prevalent in Mogaloff, and probably existed in Tantah and Cairo; while a series of rapid and unexplained deaths occurred among the workmen at Toussoum on the Isthmus of Suez Canal. Mogaloff is a village of 300 population, situated near Zagazig, and 23 deaths from "cholerine" were reported there in three days. In September any doubt as to the true character of these occurrences of "cholera" and "cholerine" was set at rest, as far as Alexandria was concerned, by a considerable outbreak of cholera, in its epidemic

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plus sensible à la radiale; le cœur ne bat que faiblement (50 pulsations par minute), les vomissements ont cessé, mais la diarrhée continue.

"6 heures.—Continuation des douleurs. La faiblesse augmente.

"8 heures.—La malade expire.

"Réunis en consultation avec les docteurs Papatheodoro et Murad Effendi, nous avons été d'accord d'attributer la cause du décès à un cas de fièvre pernicieuse, d'origine rhumatismale.

"9 heures.—Je viens d'être appelé pour donner mes soins à un individu voisin de la défunte, et qui, comme elle, se livre au blanchissage du linge.

"Je rencontre chez cet individu les mêmes symptômes que j'avais vus sur la défunte.

"27 Mai (6 heures du matin).—Je trouve le malade en meilleur état. Il a un peu réposé pendant la nuit, et la chaleur est un peu revenue aux extrémités du corps.

"8 heures.—Le malade est encore en danger, mais enfin il vit encore. Le froid a recommencé et le pouls est presque insensible.

"Midi et demi.—Je viens d'être appelé pour visiter un jeune homme, de nationalité Grecque, agé de vingt-cinq ans environ, et qui était tombé malade depuis huit à dix heures.

"La figure était bleuâtre et froide. Les joues, les lèvres, la langue, et les bras étaient également froids. Le pouls ne battait plus du tout à la radiale. Les battements du cœur étaient faibles et lents. Les vomissements arrivaient, non spontanément, mais à la suite de toute absorption de boisson. La diarrhée ressemblait presque à de l'eau naturelle. Les crampes n'existaient pas. Le malade gisait sur son lit, inquiet et hagard, ainsi que les cholériques ont l'habitude de faire à leurs derniers moments. Il avait tout à fait l'apparence d'un cholérique en état d'asphyxie.

"2 heures.—Le malade expire.

"Le petit enfant de M. Uhlrich, député sanitaire, était en convalescence d'une fièvre qui avait duré trois jours, avec gonflement des glandes tuméfiées et entre les molaires.

"Hier matin, cet enfant était couché; puis ayant éprouvé une grande soif, il se leva et but une certaine quantité d'eau, et ensuite il descendit pour jouer dans la rue. Après midi, cet enfant offrit de graves symptômes de choléra. La face était très altérée, les yeux enfoncés, les joues rentrées, les vomissements se succédaient à chaque absorption de boisson.

"La diarrhée ressemblait à de l'eau claire.

"Le soir, la partie supérieure du corps etait glacée, à l'exception, toutefois, du front. Les pieds conservaients quelque chaleur; mais, vers minuit, ils perdirent la chaleur normale, sans toutefois devenir aussi froids que les bras et les lèvres.

'28 Mai (6 heures).—Ce matin, le petit malade va mieux, mais la langue et les levres sont toujours froides. Il n'a jamais éprouvé de crampes, mais seulement il se plaint de fortes douleurs dans les reins."

"Considérations générales.—Je reconnais que tous les malades dont je viens de parler présentent la plupart des symptômes cholériques. Ce qu'il y a seulement à observer, c'est que: 1. Il n'y a pas eu de crampes; 2. Qu'il n'y a jamais eu que les parties supérieures du corps qui soient devenues froides et aient pris une couleur bleuâtre; 3. Que les douleurs aux reins étaient toujours si fortes, qu'elles arrachaient continuellement des plaintes aux malades; 4. Que chez les décédés, les pieds ne perdirent leur chaleur qu'à la dernière heure; 5. Que les douleurs cholériques n'ont été éprouvées que par l'enfant Uhlrich; 6. On peut donc conclure de tout cela que la maladie semble avoir été causée par des impressions de froid.

form, in that town. This outbreak began on the 12th September, and it was suggested that the disease had been imported from England. The value of this suggestion will be seen presently. No complete report of this outbreak has been made, and its extent must be estimated from the following meagre details. From the 18th to the 25th of September 20 cases were reported. After this date and for a short period the cases numbered, it is believed, 60 daily. On the 11th November there was said to be a sensible decline in the prevalence of the disease, and its cessation was reported on the 20th.

The significance of the occurrences in Lower Egypt here described (and which must be regarded as indications of what was happening there at the time, not of all that happened, in regard to cholera) cannot be rightly understood until like occurrences taking place about the same period in other districts bordering upon the Red Sea have been described.

On the 19th May 1866, 20 days after the termination of the religious sacrifices, and five days after the departure of the great caravan for Egypt, other caravans having started ten days earlier, cholera was again observed in Mecca; on the 23rd in Jidda; and before the close of the month at Medina. Few details are given of these outbreaks. In Mecca the date when the presence of the disease was first recognised this year is alone known. In Jidda, a case of cholera was admitted into the military hospital on the 23rd June, and from the 25th to the 30th there were nine deaths from the disease recorded. Other cases followed, but none were reported after the 30th June. A caravan proceeding from Mecca to Medina, was attacked with cholera at Bedr, apparently about the same time that the disease appeared in Mecca. At Medina it is simply known that cholera was more or less prevalent there at the period when the different pilgrim caravans left that city on their route homewards. Every caravan of which information has been obtained was infected at the time of leaving Medina. The "Great Caravan" for Egypt, left Medina on the 2nd June, and on the route to El Wedj it had 15 deaths, 12 from cholera, three from other diseases.

"Je continue donc à regarder cette maladie comme une fièvre pernicieuse déterminée par la froid, tout en convenant qu'elle ressemble beaucoup au choléra."

Dr. Flora, in a work entitled *Ærztliche Mittheilungen aus Ægypten* (Wien, 1869), republishes, with one exception, his official reports to the Egyptian General Board of Health on this disease with additional notes. The exception refers to the report relating to the first two cases described above, and of which he states, in a foot-note, he had been unable to obtain a copy in Alexandria. For this report he substitutes the following account of the cases taken from his note book :—"Gestern Mittags "wurde ich gerufen zu einer syrischen Wäscherin, 35 Jahre alt, die plötzlich 'ganz "kalt und schwarz' geworden sei (sie hatte im englischen Hotel gewaschen, aber "nur die vollends unverdächtige Hauswäsche, nicht für Fremde). *Symptome.*—Das "Gesicht eingefallen, die Augen zurückgezogen, Zunge und Lippen kalt, so die Arme "und Beine; Bauch etwas eingezogen. Erbrechen nach jeden Trunk, nicht spontan, "wässerige Diarrhöe, Radialpuls sehr schwach, Frequenz normal; leichte Waden-"krämpfe; heftige rheumatische Rückenscherzen und fast anhaltendes Heulen. "Meine diagnose im ersten Momente war Cholera. Verlauf. Um 3 Uhr: Die "Kranke etwas kälter, Erbrechen aufgehört, Püls schwächer, langsamer, Schmerzen "geringer; um 6 Uhr: Diarrhöe und Scherzen aufgehört, aber der ganze Körper "kalt, die obere Hälfte blau; um 9 Uhr Tod. 2 Fall. Ein Wascher (Araber, 30 Jahr alt.) "erkrankte gestern 5 Uhr Abends mit den gleichen Symptomen; nach Mitternacht "begann er warm zu werden, heute scheint er mit gebessert. Ich glaube heute, dass "diese zwei Fälle eher mit dem Namen *Perniciosa choleriformis* zu bezeichnen "sind; der Verlauf wird übrigens entscheiden." (Pp. 37-38.)

Dr. Flora concludes his notes of the disease which he thus named with the following observations :—

"Vielleicht war es eine hybride Form, die noch Manches von der Epidemie des Vorjahres an sich trug, aber wie alle Hybriden, der Kraft der Fortpflanzung entbehrte. In Suez halte sie unter drei Absätzen drei Monate gedauert, in allen andern Orten nur eine bis zwei Wochen." (p. 47.)

No cases of cholera occurred after the arrival of the caravan at El Wedj and in its subsequent course to Egypt. The caravans to Yembo also carried cholera with them from Medina. An infected caravan reached Yembo on the 24th May, and from that date to the 9th June there were 335 deaths among the caravans waiting embarkation there. The Syrian caravan, numbering from 5,000 to 6,000, persons reached Damascus on the 25th June, and reported that for 12 days after leaving Medina, there had been from three to four deaths daily in the caravan. It reported also that villages near the line of march were infected with cholera. Of the caravans passing into Central Arabia, and on the northern route through Jebel Shomer, to Mesopotamia, there is no information.

These facts prove that there was a general reappearance of cholera, although probably of no great magnitude in the localities of the Hejaz which had been visited by the disease in the previous year. Viewed in relation with these occurrences there can be little question that the choleraic affections which have been described in Lower Egypt were of the same nature. During the progress of the events under consideration, the International Sanitary Conference of 1866 was sitting at Constantinople, and with reference to them Dr. Bartoletti expressed the opinion that cholera had been introduced into the Hejaz from Abyssinia. On the other hand Dr. Dickson pointed out, as inconsistent with this opinion, that the data submitted to the Conference by the Ottoman sanitary agents as to the times of appearance of cholera in the Hejaz, indicated the simultaneous manifestation of cholera in several widely separated places. It is not easy to reconcile the dates given with the theory of importation from Abyssinia, unless on the supposition that the infection must have been distributed independently to Mecca and Medina. But such concurrent infection of the two cities was possible, as many pilgrims from Western Abyssinia landing at Yembo would first visit Medina, while pilgrims from Eastern Abyssinia, landing at Jidda, would, as a rule, proceed direct to Mecca; both cities, as well as the ports of landing, being exposed to the chance of infection, assuming this to exist, about the same time. Such chance of the Hejaz receiving infection existed not only from Abyssinia, as Dr. Bartoletti suggested, but also from Nubia. Although the presence of cholera in Massowah in 1866 was not recognised until June, there can hardly be a doubt from Dr. Blanc's statement,* that early in that year, the disease had been widely prevalent in the adjacent district of Tigré. From the 9th March to the 2nd June 1866, 562 passengers from Massowah were landed at Jidda from 13 ships. Of these passengers 415 were soldiers, and of the remainder the greater number it is to be inferred were pilgrims. Some of these would come from the interior of Abyssinia, and notwithstanding that a fortnight or three weeks' voyage would as a rule intervene between the time of their embarkation at Massowah and landing at Jidda, still there were certain possibilities of infection being carried by them which may not be ignored. The troops were landed from an Egyptian frigate on the 23rd of May, the day when the first case of cholera was admitted into the military hospital at Jidda, but the disease had been recognised in Mecca four days before this date. The chance of infection from Nubia was much greater than that from Abyssinia. No less than 1,613 passengers had been landed from 37 ships at Jidda, from Suakin, almost without exception pilgrims, during the same period in which the 147 passengers, exclusive of soldiers, had been landed from Massowah. Of the number of pilgrims landed at Yembo from Suakin during this period there is no information. The greater number of these pilgrims

* *Story of the Captives*, p. 65.

would be Takruris from Western Abyssinia, and other negro Mahommedans from more western countries, and in journeying to Suakin they would traverse the province of Taka, where as already described cholera was present in March 1866. Such were the known chances of infection of the Hejaz from Nubia and Abyssinia.

Lower Egypt was also exposed to infection from Abyssinia and Nubia, contemporaneously with the Hejaz, by the direct communication which is maintained through the port of Suez with Suakin and Massowah; it was, moreover, liable to infection from the Hejaz. Irrespective of the ordinary traffic with the Hejaz, there were landed at Suez, from the 7th to the 16th May, 5,066 pilgrims returning homewards. The first case of the choleraic malady described by Dr. Flora occurred on the 26th May. Cholera was not recognised in Mecca, or any part of the Hejaz until the 19th May, three days after the arrival at Suez of the last of the pilgrims mentioned, all of whom were reported in excellent health. This would appear to exclude any connection between the return of the pilgrims, at least, and the subsequent appearances of cholera in Lower Egypt. The occurrences of 1865, however, show how little faith is to be reposed upon the reports received at this period, either by the Ottoman or the Egyptian General Board of Health, regarding the sanitary condition of Mecca and of the pilgrims.

I confine myself to stating the facts so far as they are known. Both in the Hejaz and in Lower Egypt there was a wide re-appearance of cholera in 1866, dating from an early period of the year. The dates are too imperfect to admit of any definite conclusion as to the part, if any, which re-infection from Abyssinia and Nubia may have played in the phenomenon, but the possibility that such re-infection may have taken place is not to be overlooked in considering it.

In reference to this subject the relation of the re-appearance of cholera in Lower Egypt, in 1866, to cholera in England that year, suggests certain considerations of great interest. I have already shown that the prevalence of cholera in England, in 1866, was not a consequence of recrudescence of the disease imported the previous year, but of a series of re-infections from the Continent, the following instance only excepted. The re-appearance of cholera at Southampton, in July and August 1866, was the result of re-introduction of the disease by one of the Peninsular and Oriental Steam-Navigation Company's ships, the "Poonah." This ship arrived at Alexandria, from Marseille, on the 26th May 1866 (the second visit she had made to the port that month), and after 40 hours' stay she sailed for Southampton, on the 28th May, reaching her destination on the 10th June. Cases of cholera, some fatal, had been reported in Alexandria in March and April; and a case, which ended fatally, was reported on the 30th May, two days after the "Poonah's" departure for England. On the 26th–28th May, cholera was certainly present in Suez. These facts supply the link missing in Professor Parkes's elaborate investigation of the Southampton outbreak in 1866 and, it appears to me, that they complete the investigation. (*See* Maps II.–IX.)

6.—*The Diffusion to Syria and Western Anatolia.*

Syria and Western Anatolia, 1865.

I have now to describe the diffusion to the east coast of the Mediterranean, and thus complete the account of direct dissemination of cholera from Egypt in 1865.

The disease appeared at Smyrna on the 24th (? 16th) June, at Larnaka, Cyprus, on the 26th June (in the lazaretto; in the town, 7th July), at Beyrout on the 29th June (in the lazaretto; in the town, 1st July),

Smyrna, 1865.

and at Dardanelles (in the lazaretto), and also at Jaffa on the 1st July. The appearance in each of these instances it is desirable to narrate.

Smyrna.—The first reported case of cholera in this town occurred during the nights of the 24th and 25th June, but there were fatal cases of choleraic disease on the 16th and 19th June, and the epidemic most probably began here at the former date. The following was the succession of known cases until the 6th of July, after which period the disease became widely prevalent in the town. On the 16th June a boy, 14 years of age, living in the washerwomen's khan, was seized in the course of the evening with vomiting and purging, rapidly became algide, and died during the night. On the 19th June, a girl 12 years of age, living in the same khan, was carried to the Greek hospital suffering with symptoms similar to those observed in the boy, and died after a few hours illness. During the night of the 24th–25th June, a woman, M. M., living close to the Imamglou khan, which communicates with the washerwomen's khan, was attacked with manifest cholera, and died 14 hours after the first appearance of diarrhœa. On the 28th June a woman, C. H. P., who had been in attendance upon M. M. during her illness, was attacked and died 13 hours after the first observed symptom. In the course of the night of the 2nd–3rd July, the husband of M. M. was seized with cholera, and he died the following morning. The same night a sister-in-law of M. M., who had assisted, not only during her illness, but also during the illness of C. H. P., was seized and died on the 4th. On the 4th July, moreover, a son of M. M., who had fled to the town of Guez-Tépe, after the death of his father and mother, was attacked with the disease, but he recovered. The same day a dervish, who on the 24th June, according to Mahomedan usage, had washed the body of a Turk who had died on that day in the lazaretto, and was subsequently detained in quarantine there 10 days, was attacked with cholera the morning after his release, and died after a few hours illness. A woman also died this day from cholera at Fassoula, who had been in communication with the families of both M. M. and C. H. P. On the 5th two new cases occurred, one being a boatman who had communication both with the lazaretto and with vessels quarantined in the bay; the other a cousin of the woman who had died at Fassoula. On the 6th July the wife of the boatman before mentioned was attacked with cholera. The three cases last mentioned all died. Other cases also occurred on the 6th, but it is not necessary to follow them in detail.

While these events were occurring numerous fugitives were arriving from Alexandria at Smyrna. When rumours of cholera in Alexandria first reached Smyrna, early in the month, a quarantine of five days duration was imposed on arrivals from that port, but as this period of time was made to include the length of the voyage also, the detention in quarantine rarely exceeded a few hours. On the 23rd June the Austrian Lloyds' steam vessel, the "Archduchess Charlotte," landed 293 passengers at the lazaretto, one of whom was seized with cholera during the following night, and died on the 29th. A second case occurred among them on the 24th, which ended fatally the same day, and three other cases on the 25th and 26th. On the occurrence of the first of these cases, five additional days quarantine was imposed upon the passengers, else they would have been liberated on the 24th. These were the earliest cases of cholera observed in quarantine.

From the 23rd June to the 5th December 1865, 1,172 deaths from cholera were registered at the sanitary office in Smyrna. The International Sanitary Conference, 1866, estimated the number of deaths during the outbreak in this town at 2,500, and the attacks at 5,500, among a population of 100,000, reduced by emigration during the progress of the epidemic to 70,000 or 60,000.

From Smyrna the disease spread into the neighbouring district. Burnabat, a large village of 910 houses, and having an estimated population of 10,000, was attacked on the 8th July, and from that date to the 31st, 110 attacks and 72 deaths occurred. The disease also spread to a nomadic tribe, the Furaks, then encamped near the villiage. Other places which suffered from the epidemic, some more some less, were Boudja, Kassaba, Menemen, Choroskioi, Echelle-neuve, Tyrra, Denisli, Sarakeuï, Ortoxe, &c. The nomadic tribes of Fundukju and Hazziar, encamped, during the spread of the epidemic from Smyrna, between Adala and Alacheïr, were also attacked.*

Cyprus.—From the 26th June to the 13th July, 19 cases of cholera were landed from various ships at the lazaretto of Larnica, beginning on the first-mentioned date, when the sole source of infection was Alexandria. The lazaretto of Larnica is a vast stone building close to the city. On the 6th July a child, three days after entering the lazaretto, was attacked with cholera and died in the evening. The next day, the 7th July, two persons were attacked in the lazaretto, one the mother of the child before mentioned, the other a young man who had been under detention nine days. The former recovered, the latter died after five hours illness. The same day the first case happened in the city, the person attacked being the keeper of a lodging-house, where many persons going out of quarantine had lodged. The disease next spread in the city, and extended to Nicosia and other parts of the island. In Larnica (population 12,000, reduced to 4,000 by emigration during the epidemic) there were 363 deaths from cholera. The deaths from the disease in the island were estimated to number 652.

Cyprus, 1865.

Beyrout.—On the 29th June, a Jewess died of cholera in the lazaretto. This was the first case recorded at Beyrout. She had landed on the 24th June from the Austrian steam ship "Archduke Maximilian," coming from Alexandria. Three cases of cholera, one fatal, had occurred on board this ship during the voyage. On the 1st July a case of cholera was observed in the city, the patient being a person who had no relations with the lazaretto. Before this date numerous travellers from Alexandria, fugitives and others, had flocked into Beyrout, having first been subjected to a detention in quarantine of from five to ten days. Among the passengers were many poor pilgrims, sent homewards at the expense of the Egyptian Government. At Beyrout, moreover, the caravan of Persian pilgrims journeying homewards through Syria and Mesopotamia disembarked. The date of disembarkation is not stated.

Beyrout, 1865.

Following quickly upon the death of the Jewess, on the 29th June, the quarantine guard engaged in burying the body was attacked with cholera and died. Another fatal case occurred in the lazaretto on the 1st July, and a guard, specially detailed to the service of the family in which the case occurred, was attacked on the 3rd July and also died. Next the Abbé Viale, secretary of Monseigneur Valerga, the patriarch of Jerusalem, who had landed at the same time as the Jewess from the "Archduke Maximilian," died of the disease. He had been freed from detention and left the lazaretto on the 3rd July. He was attacked the same day in the city and died during the night. Another guard was also seized and died. Altogether, 30 cases of cholera, of which 15 died, occurred in the lazaretto, where there had been subjected to detention from the first news of cholera in Alexandria to the 25th July, 3,600 persons, of whom 400 were pilgrims coming from that city. During

* See as to details of the outbreak at Smyrna, "*Mode d'Invasion et de Propagation du Choléra étudié à Smyrne.* Par le Dr. D. Chasseaud. Constantinople, 1871.

the same period eight of the ships entering the port from Alexandria (in all 50) had reported 18 cases of cholera, and 11 deaths from the disease, during the voyage.

The lazaretto at Beyrout, to the east of the city, is described at the time as isolated and well ventilated, but not admitting of a proper separation of the sick from the healthy, and too small to accommodate the sudden influx of travellers from Alexandria. To relieve the overcrowding, it was supplemented by several isolated houses and an hotel situated on the opposite side of the city.

In the city the disease, after its appearance on the 1st July, prevailed for three months, and attacked 1,500 persons, causing 493 deaths,* the population being estimated at 75,000.

Dardanelles, 1865.

Dardanelles.—Here, as at Beyrout, the first cases were observed in the lazaretto, but, unlike Beyrout, the connexion between the cases in the lazaretto and the earliest cases in the town was clearly traced. Two cases of cholera, the earliest observed, occurred in the lazaretto on the 1st July. The persons attacked had been disembarked from an Egyptian ship, the "Tantah," which had arrived at Dardanelles, from Alexandria, on the 29th June. On the 12th July a soldier of the lazaretto guard was attacked with cholera and sent to the military hospital in the town, where he was placed in a ward with other patients suffering from ordinary maladies. From this date to the 14th three cases occurred in different parts of the town. The first was a boatman, who daily conveyed the quarantine physician to and from the lazaretto. The second was a dealer in eatables, who pursued his industry in the vicinity of the lazaretto. The third was a guard who had been detained 10 days in the lazaretto, and who, two days after his release, was taken ill of cholera and died in the town. Other persons attacked with the disease attached to, or in communication with, the lazaretto, were the deputy-keeper and two guards of the interior service, one of whom died. The number of persons detained in quarantine from the 29th June to the 1st August, was 2,269, and among these 16 cases of cholera occurred before disembarkation, and six after, the deaths numbering 15. In the town the disease continued until the 30th August, causing, among a population of 8,000 (less 2,000 fugitives), 369 deaths, 27 among the garrison.

Jaffa, 1865.

Jaffa.—The following account of the appearance of cholera at Jaffa was given at the close of the outbreak, by Dr. Philip of that town, in a report communicated to Her Majesty's Consul there.

The earliest appearance of the epidemic occurred on the 1st July. On that day a small Greek vessel arrived in the port from Alexandria. The same day the captain was seized with vomiting, diarrhœa, cramps, and blueness of skin, and died a few hours afterwards. The next day a Greek, in one of the crowded houses of Jaffa, was seized in a similar fashion and died the day following. Other individuals were attacked with like symptoms prior to the 4th July, and all died. None of the cases to this date had come under the observation of a medical man. After the 4th July the epidemic spread from house to house, and from street to street. At the beginning of the epidemic the population of Jaffa was estimated at 25,000, but during its progress the greater number fled from the town, many encamping in the gardens near the town, and in the plain; others seeking refuge from the disease in the neigh-

* I have followed in this account of cholera at Beyrout the statement given by the International Sanitary Conference, 1866 (*Rapport sur la Marche*, &c., p. 18), but in respect to prevalence in the city, H.M. Consul-General, in a despatch dated 21st Oct. 1865, states that the epidemic had continued until that month, and that the mortality was estimated from 1,700 to 2,000.

bouring towns and villages and in Jerusalem. At the close of the epidemic not more than 4,000 persons are believed to have remained in the town. From the 1st July to the 8th August 1865, about 3,000 cases of cholera are estimated to have occurred, the ascertained deaths numbering 580. When the disease ceased in the town it existed in some of the villages of the adjacent plain.

Alexandretta, Kara Aghash, &c.

It is necessary to add to the foregoing details that two deaths from cholera occurred on the 10th July, in the quarantine station at *Alexandretta*, and that 14 deaths from the same disease happened on board the Turkish frigate "Medjidié," at anchor off that port, at a date not stated. Alexandretta was in frequent communication both with Alexandria and Constantinople, but cholera did not appear in the town until after it had broken out at *Kara Aghash*, a large village on the coast, about three miles distant from Alexandretta, where the disease was first observed about the beginning of August. It was supposed at the time that this village had been infected from the "Medjidié."

El Arich, 1865.

While the diffusion to the coast towns of Syria above described had been in progress, cholera had spread along the principal road from Lower Egypt to the southern frontier of Syria at *El Arich*. Here the disease appeared on the 5th July, and caused from this date to the 26th September, 83 deaths.

From the starting points described on the Syrian coast cholera spread into the interior. A general narrative is alone possible from the accessible accounts of this dissemination. These, however, are sufficiently clear to admit of a tolerably accurate conception of the progress of the disease. Syria was entirely without cholera, when, in the course of June and at the beginning of July 1865, the malady began to be freely scattered from Alexandria on its coast. As soon as the epidemic had shown itself in the different seaport towns a remarkable exodus of the populations commenced under the terror of the pestilence, and the same phenomenon was observed in perhaps every town and village where the disease penetrated. In Jaffa five-sixths of the estimated population of 25,000 fled from the town; in Beyrout, two-thirds of the estimated population of 75,000. The fugitives sought refuge for the most part in the neighbouring towns and districts, and carried with them the infection of the disease. To these fugitives, rather than to the pilgrims returning from Mecca, is to be attributed the most important part in disseminating the disease in Syria, and, as will presently be seen, in certain districts beyond that country.

The interior of Syria, 1865.

Gaza, *Ramleh*, *Nablus*, and *Jerusalem* were all attacked with cholera after the flight of the population of Jaffa. In Jerusalem the disease appeared at the latter end of July and continued until the middle of November, causing 912 deaths.* Nablus is estimated to have lost 2,000 of its 8,000 inhabitants, by cholera, prior to the 23rd August.

A stream of fugitives from Alexandria had flown into Beyrout from the beginning of the epidemic in the former city; and in like manner, when the epidemic began in Beyrout very many of the population fled into the neighbouring country, and especially towards and to Damascus, and to the towns in the north, Homs, Hama, &c. Preceding or accom-

* The Report of the International Sanitary Conference, 1866 (*Sur la Marche*, &c.), states that cholera first appeared at Jerusalem on the 21st September 1865 (p. 18). I have adopted the data given in a report made by Dr. Mazaraky, Physician to the Russian hospital at Jerusalem, a copy of which was courteously furnished to Her Majesty's Consul there.

panying these fugitives were the pilgrims returning from Mecca, by way of Beyrout. Of the progress of cholera on the different routes little is known. In Damascus the disease appeared on the 1st August, in the Turkish quarter. The Syrian caravan from Mecca had entered Damascus on the 17th July, having been reported free from cholera during the forty days journey across the desert. Its arrival had been preceded by pilgrims who had travelled homeward by way of Beyrout, The city was in free communication with Beyrout, where the disease had appeared on the 29th of June; and in it many of the fugitives from that port took refuge. The Turkish quarter in which the disease appeared first in Damascus, is a place of sojourn for pilgrims who simply halt in the city; but the chances of infection from Beyrout were numerous, and the particular source of infection was not discovered at the time. Cholera prevailed in Damascus from the 1st August to the close of September or beginning of October, the estimated mortality from the disease within that period being 3,000.

North of Beyrout cholera appeared at Homs and Hama on the route to Aleppo; and in Aleppo it was first observed on the 11th August. Before this date the disease had broken out at *Kara Agash*, as already mentioned, on the coast near Alexandretta. It has been sought to show that Aleppo was infected by the Persian caravan of pilgrims returning from Mecca by way of Beyrout. This caravan did not reach Aleppo and enter the city until the 16th August, when, according to a despatch of Mr. Consul Skene, dated the 22nd August, cholera had certainly been present in the city five days. Aleppo, at the time when cholera appeared in the city, had been exposed to infection from the towns south of it and also from the coast in the vicinity of Alexandretta. Whichever the source of infection, the disease here was frightfully virulent. According to the International Sanitary Conference, 1866, it killed in the space of three months, among a population reduced from 120,000 to 90,000, by flight, 7,000 persons. But Mr. Consul Skene states, writing under date the 16th October 1865, that the deaths were computed to number 10,300.

Thirty thousand persons, it is believed, fled from the city to avoid the pestilence, the majority, there is little doubt, flying to the north towards and into the valley of the Euphrates, cholera being prevalent on the routes both to the south and the west. The probable consequences of this exodus will form the subject of a separate section (Section 7).

The interior of Anatolia, 1865.

I have already described what is known of the dissemination of the disease in the district adjacent to Smyrna. I have no information whether any dissemination took place from Dardanelles into the neighbouring district; and have knowledge only of one other outbreak in Western Anatolia, namely, in the district of Brusa. Cholera broke out in the city of Brusa in August, and caused, during this month and the month of September, 300 deaths. It appeared also at several places on the Lake of Abullonia, and at the two principal ports of the district on the Sea of Marmora, Ghio (Gemlik), and Mudania. Nothing seems to have been ascertained of the relations of the outbreak at Brusa to the appearances of cholera on the sea-coast of Marmora.

At the close of 1865, cholera appears to have died out in Syria and Western Anatolia, except perhaps in the former country at Tiberias. Here it was rumoured that the disease was present both in November and December. But in 1866 there was an outbreak at Tiberias, which began on the 24th May and ended on the 6th June, causing 54 deaths in a population of about 3,000. This year also cholera reappeared to some extent in Aleppo, in September and October, and cases were observed also in Tarsus and Adana.

Syria, 1866.

7.—The Diffusion in Mesopotamia, Kurdistan, and Persia.

I have already traced the progress of cholera in 1865 from Mecca across Central into Eastern Arabia, its diffusion upon both shores of the Persian Gulf, its appearance at the head of the Gulf in Basra, at the close of August, and its presence in Koweit and Mohammera early in September. From Basra and Mohammera cholera spread among the populations on both banks of the Shat-el-Arab, until the confluence of the Euphrates and Tigris was reached, when the upward progress of the disease was limited to the course of the former river. When cholera broke out on the Shat-el-Arab, the Arab tribes frequenting the banks of the Tigris moved into the interior, leaving the district bordering the river a desert. But the Euphrates, the great thoroughfare from the head of the Gulf for pilgrims bound for Nedjef and Kerbella, and at this time being traversed by the Persian pilgrims returning homewards along this route from Mecca, has numerous fixed populations on its banks. Following the line of the Euphrates, cholera appeared in succession at Kurna (the town at the confluence of the river with the Tigris), at Suk-e-Sheyuk, and at Samava. From the latter town, the disease, keeping strictly to the lines of communication on the river and between the different towns, pursued two routes. It was carried along the western branch of the river (the pilgrims' route) and across the Sea of Nedjef to Nedjef, and subsequently it appeared at Kerbella. It was also carried along the main course of the river-stream and appeared first at Diwanieh, then at Hillah.* Here the route of the pilgrims returning from Kerbella and Nedjef by way of Bagdad crosses the Euphrates, and on the 17th September a case of cholera, the first recognised, occurred in Bagdad, three weeks after the appearance of the disease at Basra. Eight days passed without other cases being observed when on the 25th September four cases were reported, removing any doubt which might have existed regarding the infection of the city.

In the course of September the great Arab tribe of Aneyzah, inhabiting the Syrian desert, contracted cholera, but whether from Kerbella or from Nedjef, or from infected tribes further south, is unknown.

The precise dates of the appearance of cholera in the several places attacked, in its course from Basra along the Euphrates to Bagdad, do not appear to have been ascertained, but all accessible information concurs in the order of appearance stated. The loss of life reported during the prevalence of the disease this year in some of these places was as follows:†—Diwanieh, 147; Nedjef, 366; Kerbella, 1,480; Hillah, 49; Bagdad, 17th September to 3rd December, 262.

While this extension of cholera was in progress along the course of the Lower Euphrates, from below upwards, that is to say, against stream, an extension of greater magnitude was also in progress, on both the Upper Euphrates and Upper Tigris, from above downwards, that is to say, with the stream.

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* The main stream of the Euphrates has since 1865 (if the local topography at that date is to be trusted) become lost in the rice fields which lie between Lamlum (now deserted) and Samava. Before reaching this district the volume of the river has been much diminished by numerous outflows along irrigation canals and into the vast marshes which exist on both sides of the stream below Musseyib. The main stream in this part of the river's course is now represented, according to Mr. W. H. Colvill, who visited this locality in the spring of this year (1875), by the canal of Hindieh, which opening near to Musseyib, flows through the marshes which lie between Hillah and Nedjef into the lake called the Sea of Nedjef (Bahr-el-Nedjef); and by the outflow of the Sea of Nedjef, which enters the proper channel of the river by two outlets, here forming again a considerable stream a short distance above Samava.

† International Sanitary Conference, 1866, *Rapport sur la Marche*, &c., p. 20.

Following upon the exodus of population from Aleppo in August, when cholera broke out there, as already described, and upon the passage of the Persian pilgrim caravan, the disease appeared in succession at Biredjik on the Euphrates, at Orfah on the route to Diarbekr, and at the end of the month it was reported to be present at Diarbekr on the Upper Tigris. The next month, September, cholera was reported at Anah* and at Hit,* on the Euphrates, and at Mosul and Samara, on the Tigris, in the order mentioned. Moreover, spreading westwards and southwards from Mosul, the disease appeared at Arbil and Kerkook, and in October, at Suleimanieh, near the Persian frontier. In the last-named town the disease continued throughout the winter, causing numerous deaths.

The localities mentioned in this distribution of cholera, in the upper portions of the valleys of the Euphrates and Tigris, all lie upon the routes which would be traversed by the Persian pilgrims, in their further journey homewards from Syria. Some of these pilgrims would descend the Euphrates from Biredjik to Musseyib for Kerbella and Nedjef; others would pass directly homewards by Diarbekr and the valley of the Tigris to a convenient route across the border. The localities to the north and east lie upon the most accustomed trade routes from Syria to Persia, the pilgrims being traders as well as devotees. But a like series of events probably occurred here as had been observed in the diffusion of the epidemic from Alexandria, and in its passage through Arabia, and along the Lower Euphrates. The disease seems to have spread from one new centre of infection to another rather than by continuous propagation through the agency of the pilgrims, the fugitives from Aleppo, or other infected towns of Syria first carrying the malady into northern Mesopotamia. No cholera appears to have been observed among the Persian pilgrims travelling homewards by way of Syria. (*See* Map II.)

1866.

1866.—This year, 1866, cholera reappeared in several localities of Mesopotamia, extended widely in Turkish Kurdistan, and, spreading eastwards, crossed the Persian frontier into the province of Azerbijan.

The disease had continued in Suleimanieh throughout the winter, and after an interruption in February, reappeared in that town in March. The same month it broke out at Oin on the road to Akerta, advancing into Persian territory. In March also isolated cases began to be reported in Bagdad, and 10 such cases were recorded between the 26th of the month and the 5th May. No further cases, however, appear to have been observed in this city until August, when the disease reappeared, and from that date to the 28th November, caused 172 deaths. In June, cases occurred both in Kerbella and Nedjef, and in this and the following month, the disease was reported to be severe at Jezirah and to have extended to Singar, ceasing in both places in August. There were

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* The International Sanitary Conference, 1866, in the report referred to in the previous note, mentions as affected in this extension of cholera "Anah-Hit;" and Dr. Fauvel, in his official reports on the organization of a sanitary service on the Turco-Persian frontier, (*Recueil des Travaux au Comité Consultatif d'Hygiène Publique de France*), refers to "Hitt-Annah" on the Euphrates, and he describes it (vol. 2, p. 38) as "the place where the caravans from Syria cross the river." English geographers describe, and English atlases show, two towns on the Euphrates, namely, Anah and Hit, the latter situated 80 miles or thereabouts below the former. General Chesney, when he visited Anah in 1835, travelling to it, in nineteen days, across the desert from Damascus, and first reaching the Euphrates at El Kaim, a short distance above Anah, found the town then to consist of about 500 clay houses, scattered along the right bank of the river nearly four miles, and "almost hidden in groves of date, fig, and pomegranate trees."—*Narrative of the Euphrates Expedition*, p. 66.) Hit has been known for its bitumen-springs and bitumen-coated boats since the days of Herodotus.

several cases at Basra in July, and a slight outbreak occurred at Mosul this month. There were also slight outbreaks in August at Hillah, Kifri, and Imam Moosa. In October the disease showed itself in a severe form at Mendeli, and the same month it appeared at Khanikin* on the Persian frontier, the principal quarantine station on the northern route from Persia to Bagdad. In November the disease is reported to have ceased altogether in the province of Bagdad.

In the greater number of these instances, the appearances of cholera were slight, and in none did the disease exhibit much diffusiveness. Further north, however, in Turkish Kurdistan, cholera manifested greater activity. At what particular date cholera appeared in Diarbekr is not known, but in July information was communicated to the sanitary department at Bagdad that cholera had entered Persia across the Kurdistan frontier ; and early in August there was an alarm in Aleppo of extension of cholera in that direction from Diarbekr. The movements I am about to describe must then have taken place in the first half of the year. West of Diarbekr, and lying between that town and Orfah, the town of Swerek was attacked. East and north of Diarbekr, cholera extended to the country west of Lake Van. Here it prevailed in the districts of Bitlis, Akhlat, and Bulanyk until late in the year, and spread northwards to Maka, a town lying about midway between Bayazid and Nakitchevan. North of Maka the disease, in November, was reported at Kars, and Erivan ; and east of Maka, the same month at Nakitchevan. The next month (December) cholera penetrated still further to the north, in Transcaucasia, and appeared at Tiflis.

While this extension had been taking place from Diarbekr, on the Turkish side of the frontier, and had passed northwards across the Persian frontier into Transcaucasia, further south, cholera, starting apparently from Suleimanieh, had crossed the Persian frontier. It has already been stated that in March the disease had advanced from Suleimanieh to Oin, on the road to Akerta. This last-named village is situated at the point where the road from Suleimanieh to So-uj-Bulak and Mehemetabad crosses the frontier. The disease was first heard of in Persia at So-uj-Bulak where, early in June, it was reported to be prevalent. Subsequently it spread over the districts of Solduz and Urumiah, the former lying between So-uj-Bulak and Lake Urumiah, the latter to the west of this lake. In the city of Urumiah (population 30,000), the mortality from cholera, before the close of August, was estimated at 4,000. West of Urumiah, the disease penetrated, for the first time, it is stated, into the mountain districts. On the 1st September cholera broke out at Tabriz. The disease lasted 40 days in the city, causing it was estimated, 6,500 deaths among a population of 80,000, Before the outbreak had ceased in Tabriz, cholera appeared at Resht, in Ghilan, on the south shore of the Caspian, and afterwards at Kazoin, on the road from Resht to Teheran. There was a rumour also at the close of the year of cases in Teheran. (*See* Map III.)

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* Khanikin is situated on the principal route traversed by pilgrims, coming from northern and central Persia, on their way to Nedjef and Kerbella. It is close to the frontier on the Turkish side, and is the locality of perhaps the most important frontier-station of the Ottoman Sanitary Administration. Dr. Fauvel (writing in 1850) describes Khanikin as " un bourg habité par 400 familles, et qui doit toute son " importance au passage des pélerins. Aussi, un superbe Khan á l'usage de ces " derniers et un magnifique pont en briques jetè sur l'Elvand y forment-ils un " contraste singulier avec l'aspect misérable de la localité." (*Recueil des Travaux du Comité Consultatif d'Hygiène Publique de France*, t. 2, p. 35.) Mr. Colvill visited Khanikin in 1871. His description of what he observed there is given in the account for that year. (*See* foot note, p. 110.)

1867. 1867.—Mesopotamia appears to have been almost free from cholera in 1867. No reports were received at the sanitary department, Bagdad, of its presence in any part of that province, except at Suleimanieh, where a few cases were reported to have occurred in May or June. In Persia, the disease reappeared to some extent in the province of Azerbijan, but of the particular localities of appearance nothing is known.

In spring the epidemic reappeared in Mazanderan and spreading through that province attacked Amol, Balfurush, and Sari, extended into the province of Astrabad, and broke out in that city in August. Travelling southwards from Mazanderan, the disease appeared in numerous places along the road from Teheran to Meshed in the course of summer (Khatounabad, Heivanekief, Damgan (June), Semnoon (end of summer), Lazgird, (middle of summer,) &c., and showed itself in Teheran. A report, dated the 28th August, states that before that date, 150 cases had occurred in the capital. The disease continued there until the end of October. South of Teheran cholera spread as far as Kashan; and westwards there was a slight diffusion into the district of Zerbend. Eastwards of Mazanderan and Astrabad cholera extended to Subzawar, Nichapur, and other places on the route to Meshed, and in December appeared in the latter city. (*See* Map IV.)

1868. 1868.—The progress of cholera in Persia in 1868 is of remarkable interest. Throughout the year Mesopotamia, and generally the Turkish dominions in Asia were, so far as is known, free from the disease. During the winter of 1867–68, cholera did not wholly cease in Mazanderan. In February the disease was still prevalent in Balfurush, and was reported spreading there in the environs of that town. The same month isolated outbreaks appears to have taken place on the opposite side of the country, in Serpul and Shuster, Khuzistan.

With the advancing spring cholera again became active in the north-eastern provinces. In April the disease was very intense in Bujnurd, about midway between Astrabad and Meshed, on the northern route between the two cities. In May it existed at Amol. It appeared also in Sari. Towards the close of spring and at the beginning of summer it showed itself in numerous places on the routes between Mazanderan and Astrabad and Khorassan, and between Teheran and Meshed (Khatounabad, Heivanakief, Khowar (district), Dehnemek. Lazgird, Sourkeh, Semroon and district, Shah-rud, Subzawar and district, and Nichapur). In June the disease reappeared in the east, at Meshed, and in Teheran.

Meshed is one of the sacred cities of the Shiah Mahomedans and a great centre of pilgrimage and commerce, maintaining a considerable trade with Bukhara, Balkh, and Afghanistan, as well as with the different provinces of Persia. At the time of the reappearance of cholera there in June 1868, pilgrims were flocking to Meshed, and in July, when the city was crowded with devotees and traders, the disease became very virulent. With the termination of the pilgrimage and the departure of the pilgrims a diffusion of cholera began which forms the peculiar feature of the prevalence of the disease in Persia this year. In the track of pilgrims returning from Meshed it was carried southwards to Khaf, to Birjand, to Kirman, and to Yezd, appearing in Kirman on the 20th October, and in Yezd on the 13th September. Westwards it was carried along the road to Teheran, aggravating the already existing cholera along the route. On the 5th August, a caravan of 5,000 pilgrims from Meshed entered Teheran. Up to this date the cholera present in the city had been little in amount and had shown but slight diffusiveness. There were several cases of cholera among the pilgrims when they came into the city. Following upon their entrance,

cases appeared in the city in rapid succession, and from the 7th to the 22nd August 343 deaths were ascertained to have occurred. The disease next spread in the villages near to the capital, and extended westwards to Hamadan, and southwards to Ispahan, appearing in the former town on the 20th November, and in the latter at the end of the same month.

At Hamadan the disease was still prevalent at the close of the year. At Teheran the outbreak had well nigh ceased about the middle of December. From the 27th November to the 15th December, 234 deaths were known to have occurred there. The total loss of life during the prevalence of the disease does not appear to have been ascertained. Cholera prevailed in Meshed during the three months June, July, and August, extending to the neighbouring villages. North of Astrabad the disease broke out with much severity at Ak-kaleh on the Gurkan River. A body of soldiers coming from Ak-kaleh, at the time the disease was prevalent there, re-introduced the malady into Astrabad, where it caused 100 deaths among the troops, and 50 deaths among the civil population. Still further north, on the Attrek, cholera broke out in the course of the autumn, among the Yomut Turcomans. (*See* Map V.)

1869.—The diffusion which had begun from Meshed the previous year continued, in 1869, along the various routes which cholera had most conspicuously followed. In Khorassan, and especially in Yezd, the disease was still active in the autumn of this year. Hardly a locality traversed by the route from Meshed to Teheran, and visited by cholera in 1868, escaped another visitation of the disease in 1869. In Teheran there were several cases of cholera in April, but in June the malady once more became epidemic there, the deaths during part of July numbering 80 daily. This outbreak continued until late in the year. South of Teheran, cholera was present in Kum in February, in Kashan in May, and was active in Ispahan in July and August. From this point which had been reached by the disease the previous year, cholera was carried still further south to Shiraz. In this city the disease appeared about the 15th July and continued until the 16th August. During this period, according to Major St. John, who was at Shiraz at the time, the mortality was probably 2,500 out of a population estimated at 35,000. From Shiraz the disease was disseminated in the neighbouring district and along the road to Bushire. At this last-named town and in villages adjacent cholera appeared in October, but it is undetermined whether as an extension from Shiraz or from some other source. 1869.

On the western route from Teheran, cholera had continued at Hamadan from the previous year until the beginning of January 1869; and in the course of this month, towards the end, it broke out at Kirmanshah and in three weeks caused 100 deaths, among a population of 30,000. In February, also, a group of cases occurred at Nassur opposite Fao-el-Jub, near the mouth of the Shat-el-Arab, five deaths from cholera occurring there on the 16th of the month, and three on the 17th.

Not until August was any further activity of the disease observed along the route by way of Hamadan and Kirmanshah across the frontier. But in August, contemporaneously with an influx of pilgrims coming from the interior, and on their way to Kerbella and Nedjef, the disease re-appeared at Kirmanshah; and it subsequently broke out in several localities along the route traversed by the pilgrims, and in the two sacred cities. Cholera also appeared and prevailed with some severity in the district of Khalis, on the Turkish side of the frontier, and lying between Bagdad and the frontier quarantine station at Khanikin. In Bagdad, on the

14th October, a case happened in a family lately arrived from Persia, and it was followed at intervals by other cases. Except in Kerbella and Nedjef the disease, in this extension into Mesopotamia, did not manifest much activity. From the 10th October to the 12th December, there were recorded in Bagdad 39 deaths from cholera, in Imam Musa 18, in Kerbella 210, and in Nedjef 343. In the course of December several cases of cholera were reported at Mohammera, at Diwanieh (among troops stationed there), and at Suleimanieh.

In the north and east of Persia this year, Kasbin, Tabriz, and Tadjirsh did not wholly escape; the provinces of Ghilan and Mazanderan were still infected to some extent; the soldiery in Astrabad again suffered; there was a virulent outbreak at Anzan, a village in the district; and at Meshed there was a fresh outbreak, at the end of August or beginning of September, which at one period of its progress caused from 50 to 60 deaths daily. Late in December, Teheran, and the provinces of Ghilan and Mazanderan were reported to be entirely free from cholera. (*See* Map VI.)

1870.

1870.—At the opening of 1870 cases of cholera were still occurring among the troops at Diwanieh on the Lower Euphrates, but elsewhere in the province of Bagdad no other occurrences of cholera took place until September.

In April the disease broke out in the neighbourhood of Kirman, in South Persia, a continuation doubtless of the extension of the two previous years in Khorassan and Yezd. Cholera was prevalent in the province of Kirman in August, and in November, about the middle of the month, it appeared at Bunder-Abbas, on the coast of Mogistan, south of Kirman, where it was stated to have been introduced by a caravan from Kirman. Here the disease caused the death of from 300 to 400 persons in three weeks. In August cholera reappeared in Kum, Seidabad, Hamadan, and Kirmanshah, but in the latter place only seems to have been serious. There, from the 3rd September to the 19th, 257 deaths occurred. In the course of September cases of cholera occurred at Kirzabad on the Persian side of the Turco-Persian frontier, and at Khanikin* and Kuzlrobat, on the Turkish

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* "On my way from England last autumn to rejoin my appointment, by Russia and Persia, I had to spend ten days in quarantine on the frontier at Khanikin, and I can best give an idea of Turkish quarantine by trying to sketch what I saw. Khanikin is a town of about 2,000 inhabitants. Here the river Diayalah, crossed by a stone bridge, separates Turkey from Persia, and at the Persian end a plot of ground bounded on one side by a canal was marked out as the quarantine camp, and here for two months before my arrival as many as 5,000 travellers, Asiatic Russians, Afghans, and Persians, had at the same time been encamped. Each company, on coming in, was supposed to pitch its tents a few feet apart from the previous arrivals, though the people mixed freely together. I arrived half an hour before midnight, and the stench from dead quadrupeds and all manner of abominations was frightful, but that was not all; for if a person were found dead from cholera, his company had to begin the quarantine afresh, the result being that no sooner was the breath out of the dying man than his friends scraped a hole in the ground under the tent and pushed him in, while after them another company would arrive, pitch on the same ground and probably do the same. In one case the friends were in such a hurry that they left the dead man's beard protruding; the jackals came, and next morning his bare jaw bones were sticking through the ground. No account is kept of the arrivals, and no care whatever is taken of the travellers, but that is no fault of the sanitary officers, for they have not the means. While I was there the dead body of a Persian was found, and the Persians raised a storm which threatened to be serious,—for they were numerous and well armed,—when they heard they had to begin quarantine anew. The Persian Agent sided with his people, by declaring the man had died of fever, while the Turkish authorities took the other view of the matter. They agreed to refer the affair to myself. I found them

side. On the 21st September the Shah left Teheran on a pilgrimage for Kerbella and Nedjef, his camp containing 10,000 men and 13,000 animals. Cases of cholera occurred in the camp from time to time for several days after the march commenced, but before the camp reached Kirmanshah on the 27th October, it was reported free from disease, and it was suffered to pass the frontier without being subjected to quarantine. After the departure of the Shah from Teheran there was a sharp outbreak of cholera in the capital, which continued during October and November, the deaths at one period being from 130 to 140 daily. This outbreak was attributed to the disinterment of about 300 corpses for the purpose of carrying them to Kerbella and Nedjef, for re-burial there in the sacred soil, according to a practice of the Shiah Mahomedans. The majority of these corpses were of persons who had died of cholera. The Shah issued an edict this year that in future this practice should be limited to corpses that had first been buried at least five years.

Except two deaths from cholera in Bagdad in October, and a slight appearance of cholera in the district of Khalis the same month, no manifestation of cholera followed upon the passage of the Shah from the frontier to the sacred cities, and no cases were recorded in Kerbella, and not until later in the year in Nedjef. North of the Shah's route, 20 cases were reported at Hibhib, a village 10 hours distant from Bagdad; and a singularly fatal outbreak occurred at Tomar, near Suleimanieh, which is stated to have caused 775 deaths in 11 days (15th to 26th October).

In December a virulent outbreak occurred at the village of Soodeah, near Shiraz.

Early in the same month three cases of cholera were reported to the Ottoman Sanitary Administration at Bagdad as having occurred in Nedjef.* From this period no further information was received of the presence of cholera in the province until the beginning of March 1871. (*See* Map VII.)

On the 10th March 1871, the appearance of the disease at Kurna 1871.

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ranged—the Persians on one side of a ditch and the Turks on the other, while a dead body, stark naked, lay in the bottom. The Persian account of the dead man's case, though very circumstantial,—that he had been seized with fever many days from the frontier and had died from exhaustion,—I could see was not expected to be believed; but as no orders had been issued to the travellers, I proposed, as the company had still eight days to remain, that this case might be overlooked, while a proclamation should be issued to all that every one who died should be considered to have died of cholera, unless the illness had been previously reported. The decision appeared to satisfy both sides. I was very much struck with the energy and perseverance of the European officer here, but what could he do, single-handed, amongst 5,000 constantly coming and going, men from the north, not by any means in the best of temper, and whose language he could not understand? The provisions purchased through intermediates were dear. This camp, varying from 3,000 to 5,000, was simply a hot-bed of disease; while it did not prevent cholera entering Turkey by that road, for it appeared at Kizil Robat, a village of about 800 inhabitants, 16 miles on the way towards Baghdad, and for 10 days five to six people died daily; and yet this camp, behind the disease, was kept up for a couple of months after that, while no quarantine was established between Kizil Robat and the interior, that is towards Baghdad."—Mr. Colvill, "*Short Report on Cholera Epidemic in Turkish Arabia in* 1870-71."—Transactions of the Medical and Physical Society, Bombay, No. XI. 1871, Appendix, p. xxxix.

* "Were supposed to have happened." Mr. Colvil, Report to Indian Medical Department. *Transactions of the Medical and Physical Society, Bombay*, No. XI, 1871, Appendix, p. xxxvii.

was notified,* and on the 17th at Basra. But in February, cholera had broken out at Bushire, and subsequently it became widely prevalent on both shores of the Persian Gulf and Gulf of Oman.

The disease, as already stated, had appeared on the eastern shore of the Persian Gulf, at Bunder Abbas, about the middle of November. It is believed to have been carried there by a caravan coming from Kirman. The person first attacked was an attendant of the governor, who having been sent to meet the caravan and receive letters, was seized with cholera on his return to the town. Cholera prevailed in Bunder Abbas four weeks, causing, it is estimated, from 300 to 400 deaths. The dates of the subsequent appearances of the disease on both shores of the two gulfs are not known. At Bushire the malady had assumed serious proportions on the 28th February, and it continued to prevail until May. The number of deaths occasioned by it in the town is believed to have been not less than 2,000. The villages in the district adjoining the town also suffered from the disease. In May, cholera was prevalent at Deyer, 90 miles south of Bushire, and at Bahrein, on the opposite coast. In June it was present at Khatif; and a report from native sources stated that the deaths in Bahrein had fallen from 120 daily to three or four. In July, Lingah, on the east coast, and Maskat, on the west coast, were reported to be infected with cholera. The deaths from the disease were numerous in Khatif this month. In August, cholera re-appeared in Bahrein. In September the disease was reported to be generally diffused among the districts of the littoral. On the eastern coast the prevalence of cholera this month was particularly noted at Shargah, Ras-el-Khymah, Lingah, Bassidore, Kishm, and in the villages adjacent to these places.

While this considerable extension of cholera was in progress upon both shores of the Persian Gulf, and of the Gulf of Oman, a hardly less considerable extension was proceeding along the rivers Shat-el-Arab, Euphrates, and Tigris. I have already noted the appearance of cholera at Kurna and Basra in March 1871. The same month also the disease was reported at Fao-el-Jub, near the mouth of the Shat-el-Arab, and Suk-e-Sheyukh on the Euphrates. It was noted at the time that cholera was mainly prevalent in these places among Persian pilgrims on their way to Nedjef. Bushire, where cholera during this month was prevailing seriously, is an important port of departure for pilgrims journeying to Nedjef and Kerbella. There is no information of the progress of cholera in Irak Arabi in April, but in May the disease was prevalent among the Beni-Lami Arabs who occupy the districts on both banks of the Lower Tigris, below the beginning of the Shat-el-Hie. In June cholera was present in the two pilgrimage towns of Nedjef (Meshed Ali) and Kerbella (Meshed Hussein) on the borders of the Syrian desert, at Diwanieh and Hillah on the Euphrates, at Kut-el-Amara, Amara, and Bagdad, on the Tigris, at Mendeli near the Persian frontier, and among a Turkish expeditionary corps, destined for Central Arabia, in the vicinity of Basra. On the 9th June, 40 cases of cholera and four deaths from the disease were reported from Nedjef. The duration and degree of prevalence of the disease in Nedjef is not known. In Kerbella the mortality must have been large, and the disease was not extinct there in December. In Bagdad 140 deaths were reported between the 20th June and 25th September; and in November cholera reappeared there among a body of troops recently arrived from Aleppo. The disease died out in the city apparently in December.

An interesting episode of the extension of cholera on the west of the

* "Four or five people died, and the disease ended on the 15th."—Mr. Colvill, Report cited above, p. xxxviii.

Euphrates, in June, was the carriage of the disease into the Jebel Shomer district, Northern Arabia, by a body of Persian pilgrims leaving Nedjef early in the month. This episode and its consequences will be related in a separate section. (*See* (a), p. 114.)

In July cholera appeared at Suleimanieh and Khanikin,* and in the former town it prevailed with much severity. On the 29th of the next month (August), 188 deaths were reported to have occurred that day in Suleimanieh; in Khanikin from the 2nd to the 11th August, 20 deaths were reported.

In August a very severe outbreak of cholera happened at Kerkuk after a violent rain-storm. Not less than 1,200 deaths, it is believed, occurred within a period of 20 days, among a population estimated at 25,000.

In November cholera was reported in Mardin at the extreme north of the province of Bagdad, in Revanduz, and in Mosul.

I have described the prevalence of cholera on the littoral of Southern Persia in 1871, in conjunction with the prevalence of cholera on the littoral of Eastern Arabia, the topographical relations appearing to me of more interest than the territorial. I return now to the further progress of cholera within the Shah's dominions this year. It will be remembered that 1871 was a year of great famine in Persia. In several districts of the interior and the north, cholera added to the miseries of dearth. In May the disease reappeared in Teheran and Shiraz. The outbreak at Teheran is described as being of less severity than preceding outbreaks. It ceased in July, and the greatest ascertained daily mortality from the malady was said to be 120. In June cholera was present at Turco-mantchai, near Tabriz, and it prevailed with great severity at Kashan and Sheriff Shiraz. In July the disease was prevalent in Zendjan, Kazom, Ardetil, Hamadan, and Tabriz. On the 29th July the mortality from cholera in the last-named city was reported to be 120 daily. In August the disease was generally prevalent throughout Azerbijan. At the beginning of the month the deaths in Tabriz had increased to 200 daily. In October, cholera was reported prevalent at Urumiah, Selma, Hufa, Amol, and Astrabad. From the province of Astrabad the disease is believed to have extended into Central Asia. The prevalence of the disease there in 1871–72 will be considered in a separate section. (*See* (b), p. 116.)

While the movements of cholera in 1871, above described, were in progress in Eastern Turkey in Asia, Eastern Arabia, and Persia, the disease also existed in Western Turkey in Asia. It broke out in the district of Brusa in June, and at a later period it appeared at Ismid, Kutaye, Amassia, and Samsun. The chronological relationship of these appearances was with the European extension of the malady this year, and they will be described with that extension.

1872.—Cholera is reported to have ceased altogether in the province of Bagdad in January 1872; and no information as to the existence of the disease in other parts of Turkey in Asia has been received from the close of 1871 until the present year (1875). In 1872 two outbreaks of cholera appear to have been alone reported in Persia. One of these occurred in Hamadan, beginning on the 8th July and ending on the 31st August. The greatest daily mortality in this outbreak was 23. The other outbreak occurred at a place designated in the official despatch Meghes. Since 1872 cholera has not been officially reported in Persia. 1872.

* See foot note to p. 117.

(a.) *The Diffusion in Arabia and Nubia in* 1871–1872.

The diffusion in Arabia and Nubia in 1871 and 1872 was an offshoot of the diffusion during the first-named year in Irak Arabi. On the 19th June 1871 cholera appeared in Haiel, the principal town of the Jebel Shomer district, northern Arabia. The disease is reported to have been introduced there by a caravan of Persian pilgrims bound for Mecca, and coming from Nedjef, where cholera was prevalent at the time of its departure. From Haiel the disease was propagated along the caravan route to Medina, by way of Khaiber. Cholera appeared at Khaiber on the 14th July, having been brought there by an infected Bedouin tribe. On the 10th August the disease appeared in Silsilah, midway between Khaiber and Medina ; and in September it broke out in Medina, first attacking a body of troops who had newly arrived in the city from Khaiber. On the 24th September the Nejediye caravan, last from Medina, entered Mecca with sick from cholera among the persons constituting it, and on the 21st October the disease broke out in the city, and prevailed there more or less until the 25th January 1872, when it apparently ceased. After the appearance of the disease in Mecca a body of troops marching thence to Confodah, on the sea-coast south of Jidda, conveyed the disease with them, infecting the garrison of Confodah, where cholera appeared on the 18th November. At the end of October, when the influx of pilgrims had begun, one or two doubtful cases of cholera were reported in Jidda ; and on the 19th December the disease appeared in Yembo, north of Jidda, supposed to have been introduced there from Medina.

At the beginning of 1872 cholera was still active at Confodah and, as already mentioned, Mecca. On the 8th January it was reported that there had been 295 deaths from cholera among the troops at Confodah in the preceding fortnight, and 18 deaths among the civil population. Early in January a body of troops, numbering 5,000 men, was sent from Confodah to Hodeida by sea, cholera existing among them at the time. When these troops reached Hodeida they were not suffered to communicate with the town, but were marched 20 miles away from it, and there encamped and isolated until the disease died out. Early in February the general in command of these troops reached Hodeida from Confodah, bringing with him a detachment of 800 men also infected with cholera. This detachment was at once admitted into the town, and the disease spread to the garrison and the civil population, and continued to prevail among them until late in March.*

In January, while cholera was still prevalent in Mecca, a caravan leaving that city for Medina, by way of Bedr, was attacked with the disease on the second day of its journey, and 80 persons lost their lives in two days.

On the 27th February cholera reappeared in Mecca, no cases having been noted since the 25th of the preceding month. Within this interval the pilgrimage of 1872 had been accomplished and the great mass of the pilgrims had left the city and its environs. The days of the religious rites were from the 19th to 23rd February, and it is estimated that on the principal day there were assembled together 110,000 pilgrims, chiefly Bedouins. During the rites and when the congregation of pilgrims was greatest, no cholera was observed; but a disease, described as "an "epidemic fever with rheumatoid symptoms and not fatal," prevailed extensively among them. This malady was no doubt *dengue*, which had

* *Fauvel*, Rapport sur la Marche du Choléra en Orient depuis le mois de Janvier 1872. (*Recueil des Travaux de Comité Consultatif d'Hygiène Publique de France.* Tome iv., p. 63, 1875.)

previously been prevalent on the East African coast, and which had appeared in Zanzibar immediately after the cessation of cholera in that island, in July 1870.

Cholera at the time of reappearance in Mecca was first observed among Takruri pilgrims—Mahomedan negroes from Africa—who had not departed. The history of the caravans which had already left Mecca, so far as this is known, proves that cholera was becoming active at the moment of dispersion of the pilgrims. The Damascus caravan, numbering 4,000 persons, took its departure on the 25th February. Two days afterwards, that is to say on the 27th, the day when cholera was first observed among the Takruri pilgrims still remaining in Mecca, cholera broke out in the caravan. Other caravans were also attacked with cholera on their route to Medina, and it is estimated that of 25,000 pilgrims who travelled homewards by this route, 4,000 lost their lives from the disease between Mecca and Medina. Cholera, according to the official reports, reappeared at Medina on the 8th March; but the native medical officers attached to the Damascus caravan stated, that when that caravan reached Medina on the 10th March, they found cholera very prevalent among the pilgrims there. Cholera prevailed in Medina until the 3rd April, causing 1,800 deaths among the inhabitants of the city. The Damascus caravan was still suffering from cholera when it reached Medina, and it did not become free from the disease until it arrived at Mudayn-Saleh on its further course. Altogether cholera destroyed, it is believed, 400 lives in this caravan during its homeward journey. The Grand Caravan of Cairo, numbering 1,130 persons, reported 24 deaths from cholera between Mecca and Medina; and after leaving Medina until it reached El Wedj, five deaths from ordinary ailments only.

Arabia, 1871-72.

Cholera reappeared in Yembo, brought there it is believed from Medina in April; but Jidda and the sea-route appear to have been quite free from the disease.

No cases of cholera were reported at Hodeida after the 25th March; and none at Mecca after the 18th April.

After the news of the reappearance of cholera at Medina reached Egypt, ships carrying pilgrims from the Hejaz ports, were subjected to 20 days detention at El Wedj, and the pilgrim caravans going by that route to a detention of 15 days. A detention of 10 days at Moses' Wells was also directed for the caravans, in the event of any suspicious sickness or death among them during the journey from El Wedj to the vicinity of Suez.

Nothing appears to be known of the progress of cholera in Yembo after its appearance there in April. No subsequent outbreak was reported in Arabia, but in June the disease broke out on the opposite coast of the Red Sea. Cholera appeared there first among a body of Soudani troops, which left Suakin for the interior, mounted upon camels, and among the camel attendants, about the middle of the month. On the route to the Bedouin town of Hatanie, district of Manderieh, province of Taka, 12 or 13 days' journey for camels from Suakin, and which was reached on the 30th of the month or a little earlier (for the official details of the movement are wanting in precision), nine of the soldiers died from cholera, and 20 of the attendants. Moreover, the disease was communicated to the villages or towns of Tokar and Helet-el-Hatinie, through which the troops passed; as also to Hatanie after their arrival there. It is stated that at the time the troops left Suakin there was no cholera in that port, nor did any appear afterwards. But the reports give no information as to the previous history of the infected troops, or of the movement of pilgrims and others returning from the Hejaz, especially of the Takruris; and the reporters do not

Nubia, 1872.

appear to have been aware of the extent of prevalence of cholera among the pilgrims on the route from Mecca to Medina, of the serious outbreak in the latter city in March, and of the presence of the disease in Yembo in April. Suakin was, indeed, the one port on the western coast of the Red Sea peculiarly liable to infection from Yembo; and the line of dissemination of the disease and time of appearance in the province of Taka, while consonent with the theory of infection, is hardly reconcilable with a suggested theory of development from exceptional meteorological conditions, not peculiar to Nubia at the time but common to vast tracts of adjacent countries. The absence of details such as we have indicated implies that the reporters had not the clue in their hands and had failed to discover it. It detracts, moreover, from the value of the statement regarding the entire freedom from cholera of Suakin at the period when the infected body of troops or of camel attendants left it, and for a short time previously.

Cholera, after the appearance described in the province of Taka, spread to some extent in the adjacent provinces of Berber and Dongola. The following is the official return of the periods of prevalence and loss of life from the disease in the several provinces:—

Nubia.—Cholera, 1872.

Provinces.	Dates of Prevalence.	Monthly Mortality.	Total Mortality.
Taka	30th June to 2nd September	240	397
	30th October to 4th November	157	
Berber	17th August to 2nd September	478	691
	3rd September to 2nd October	114	
	3rd October to 31st October	99	
Dongola	3rd September to 2nd October	623	882
	3rd October to 31st October	250	
	1st November to 30th November	9	
			1,970

Cassala and Tokar were both affected during the later period of the outbreak in the province of Taka. According to information received at the time, the disease appeared in Cassala on the 11th October, and did not cease there until the 30th November, during which period there were 165 deaths, of which 14 only occurred after the 10th November. In Tokar the disease reappeared on the 19th October. This outbreak was confined to troops and their families, and continued until the 25th November, during which period there were 65 cases and 35 deaths. It will be observed that the province of Suakin, in which Tokar is situated, is not mentioned in the summary return; and that the information as to Cassala would make the later period of the outbreak in the province of Taka of greater duration and more fatal than the summary return shows. (*See* Maps VIII., IX.)

(b.) *The Diffusion in Central Asia*, 1871 *and* 1872.

While cholera in 1871 was extending westward from Irak Arabi into Arabia, it is probable that it was also extending eastward from Persia into Turkestan. The following account of this diffusion is, with the

exception of two or three particulars obtained from Indian sources, taken from an article by Dr. M. Souvorov, Councillor of State and Inspector of the Military Medical Circuit of Turkestan, published in the *Turkestan Gazette*.*

Dr. Souvorov is enabled to state positively, as the result of his inquiries, that cholera was present in Bukhara in 1871, although it did not show itself there in a very active form in that year. He infers that the disease had extended into Bukhara that year from Persia. I have already described the prevalence of cholera in the province of Astrabad in 1871, and it is not improbable that Dr. Souvarov's inference is correct. But in 1869, cholera, according to Dr. Bryden,† was prevalent in Jellalabad and Cabul in September; and late in November it had not entirely ceased. There may have been extensions from Eastern Afghanistan through Kunduz into Bukhara, but it is hardly likely that two years continued prevalence of the disease in that country would not have come to the knowledge either of the Russian or the Indian authorities.‡

At the beginning of May 1872,§ cholera broke out at Djisack, in Russian territory. Dr. Souvarov believes the disease to have been introduced there from Bukhara, but whether at the time of its commencing activity in 1872 or at the close of 1871 is undetermined. He thinks the former alternative more probable. From Djisack the disease appears to have spread as from a centre. To the south it extended to Samarcand, Sehaar (Shehri Sebz?), Kitab, Karshi, Hissar, and (which Dr. Suvarow was unaware of), south of the Amu Daria, to Balkh and westward of that city to Akela. Eastward and southward of Djisack, Tashkurghan, Kunduz, Hazrat-Imam, Gori, and the intervening districts

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* "The appearance and spread of the Epidemic of Cholera in Central Asia in 1872." The *Turkestan Gazette*, 13th March 1873.

† *Report on the General Aspects of Cholera in* 1869 (Bengal Presidency), p. 36.

‡ The International Sanitary Commission of 1866, in its "Rapport sur les "Mesures à prendre en Orient pour prévenir de nouvelles invasions du Cholera en "Europe," observe of Bukhara (p. 62):—"La Boukharie a été souvent visitée par le "cholera. Il résulte des renseignments recueillis sur ce point par M. le Dr. "Polak, que le plus ordinairement, la maladie y vient de *Mesched* avec les caravanes "qui, de cette ville, établissent des relations commerciales importantes avec "Boukharie. Cependant ce n'est pas la seule voie; car il parait établi qu'en 1828 "et en 1845, le cholera y fut importé de l'Afghanistan par la route de Caboul."

With regard to the above asserted frequent prevalence of cholera in Bukhara, the following statement of Dr. Souvorov, in the paper referred to in the text, should be compared. He writes:—"It appears that cholera (in the Tadjiski dialect '*voba*,' "and in the dialect of Ousbeck, '*vuliat*,') did not exist among the populations of "Central Asia for 25 or 27 years, commencing with the years 1846–48, that is, the "time of the second great outbreak of cholera which originated in India and "travelled through Asia and Russia, and the whole of Europe, after the first great "epidemic of the years 1830–32. The old inhabitants of the above-named places "[Djisack, Ura-Tube, Khodjent, Samarcand, Tashkent] tell us that in the years "1830–32, cholera cruelly attacked the population of Central Asia and was spread "over all the Khanates. In the years 1846–48 the disease was considerably weaker, "and from that period until 1872 they had not known of its existence or seen "anything of it. We likewise did not hear of its existence when we were in the "steppes of Central Asia in 1857. . . . . At least one fact is certain that "the epidemic of cholera of the year 1872 as regards the population of Central "Asia and our own territory there is a new epidemic, the third since the periods "1830–32 and 1846–8, from which latter period until 1872 they had been free from "the disease."

§ The *Turkestan News* of the 25th July 1872, publishes a return showing that 675 deaths from cholera occurred in the Province of Kouraminsk from the 8th to 15th April 1872. The same journal of the 1st August notes the cessation of cholera in parts of this province in July.

were affected. Westwards from Djisack the disease returned upon its steps to Bukhara by two routes, Nourata on the north, and Katy-Kourgan on the south. Passing westwards and southwards from Bukhara, cholera entered into the Khanate of Khiva. Eastwards and northwards from Djisack, the disease travelled into Kokan by way of Ura-Tube and Khodjent, also by way of Chinaz, Tashkent, and Chemkend, and on this latter route it reached the district of Tokmak. Cholera was generally diffused throughout the Khanate of Kokan. From Chemkend, cholera extended to the town of Turkestan, and thence it followed the Syr Daria to Kasalinsk.

The further the disease travelled from Djisack, the less active it became. At the beginning of November it ceased entirely in Tokmak and on the Khivan frontier, the extreme points of its extension; and in the course of that month it would appear to have died out over the whole area of diffusion. Dr. Souvarov does not give any general account of the probable mortality occasioned by the epidemic where this could be estimated; but it appears to have prevailed with considerable severity in the infected Khanates.* (*See* Maps VIII. and IX.)

The following observations of Dr. Souvorov on the epidemic of 1872, in Central Asia, will be read with interest:—

"During the course and spread of the disease the following circumstances individually invite attention:—

(*a.*) *The return (course) of the epidemic from our country into the dominions of Bukhara*, whence it came to us quietly and imperceptibly, whereas it went back with such cruelty that the Beys of the neighbouring Emirs of Bukhara, being panic-stricken at the number of deaths among the people, applied to us for assistance, which was given, and with which they were extremely satisfied. We think that this phenomenon may be thus explained:—When the epidemic (Persian) was approaching us, it was in its period of decline and cessation, whereas when the epidemic (the Central Asian) was returning it was in its period of development.

(*b.*) "Spreading itself principally along the highways, postal-tracts, and in the valleys of rivers, the epidemic severely attacked the settled and half-nomadic population of Bukhara, Kokan, Samarkand, Tashkent, and the district of Zaravshansk and a part of Syr-Daria. Cholera extended likewise to the settled population of the mountains, some seven thousand feet in altitude above the level of the sea; for instance, in the districts of Kouraminsk and Khodjent. The further the Nomads were from the road and postal communications, the less they were attacked by cholera, and when in the midst of steppes they did not have it at all. On the other hand some steppes such as from Djizack to Chinaz, from Turkestan to Kasalinsk, from Chemkend to Tokmak, were not free from the epidemic. True these are situated in the 'rayon' of the postal lines, therefore evidently they owed the cholera to the postal communications and postal stations, fortresses, and forts situated along these postal tracts. Having in view the last fact, a word may be permitted on the bearing of the conclusion come to by the Sanitary Conference at Constantinople: '*As regards the safe-guard afforded by vast steppes against the spread of cholera*,' when the time comes that we shall have in our steppes a well organized postal [posting] communication, *i.e.*, the possibility of being rapidly conveyed from one settled point to another, from one fortress or station

* According to the *Turkestan News* of the 27th June and 1st August 1872, cholera appeared among the natives of the province of Syr Daria on the 30th May; at Tashkent on the 18th June, and at Khodjent on the 20th June. In the town and district of Djisack, 251 deaths from cholera were returned from the 30th May to the 15th June; and 142 deaths from the 3rd to the 20th July. In the town and province of Khodjent there were 455 deaths from the 10th to the 20th July; in the town of Chemkend, 130 deaths from the 5th to the 20th July; in the town of Turkestan 25 deaths from the 13th to the 19th July; in Perovsk, 1 death up to the 16th July; and in Tashkent (estimated population, 40,000), 3,953 cases and 2,503 deaths from the 19th June to the 28th July.

to another. In my opinion the steppes, at present, cannot of their own accord play, in this respect, any separate part, and they form a barrier against the spread of cholera, only because they have no postal tracts and settled points, and cannot therefore give to the spread of the epidemic any infectious centres. But when the steppes will have such communications, it is difficult to say what could serve to hinder, "caeteris paribus," the spread of cholera in the steppes and out of them. From our observations we can bring forward examples where insignificant postal stations placed in the midst of steppes, served as points of infection for a rapid spread of the cholera, and had these not existed the epidemic, "lege artis," would hardly have reached from Djisack to Kasalinsk and Tokmak, through the great steppes. When the question as to the safeguard presented by the vast steppes against the spread of cholera was under discussion, the time was so to say a nomadic one; but now we are under different conditions, we live now in the time of post [posting] offices and stations and have already in the steppes settled points.

As a proof that there really must be a difference in the spread of cholera in the steppes during the nomadic period and the postal period, the following circumstances may be pointed out:—I have already said that in the period of 1846–48 cholera existed among the population of Central Asia, now subjected to us. In 1848 our first fort was erected at the mouth of the Syr-Daria, and in its neighbourhood at that time there was no cholera. I allude to this because when I was ordered to serve in 1857 in this fort, I found no trace of the existence of cholera in examining the papers of the lazaretto of the fort, and I heard nothing on the subject either from my predecessors whom I knew personally, or from the local inhabitants, the Kirgiz. At present, under different conditions, it is seen that the epidemic of cholera from Djizack reached without any hindrance, gradually, so to say, with regular intensity, the town of Kazalinsk, *i.e.*, where it did not exist at all in the year 1848.

(*c.*) A detachment of young soldiers, about 3,000 men, sent to complete the strength of our regiments, arrived here when the cholera already existed at Kazalinsk and Perovsk, and was attacked by it very feebly, the number of those attacked being very few. When the detachment approached Chemkend and Tashkent, where cholera had ceased by that time, the disease also ceased in it.

(*d.*) The steamer "Samarkand," on leaving (with a barge) Chinaz, when the epidemic existed there, received (after a few days' sailing) from other vessels four cholera patients, two of whom died during the voyage, and two subsequently recovered and were conveyed to Petrovsk. This steamer thereby somewhat overtook the regular course by land of the epidemic."

Dr. Souvorov adds the following note respecting the disinfection of latrines and cholera evacuations:—

"According to some surgeons of Turkestan, and my own personal observations during the epidemic, and also in the year 1866 under other circumstances, the daily covering of the evacuations with a layer of small dry clay earth, about a foot in thickness, deserves special attention among other precautions, owing to its effectiveness and its practicability, especially in our country."

IV.—The Recurrence of Cholera in Europe in 1869, and Subsequent Diffusion on the Continent during the Five Years 1870–1874.

Re-appearance of cholera at Kiev, 1869.

With the exception of three small outbreaks, two occurring in the district of Lipowetz, Government of Kiev, Russia, the third at Relinghausen, in Essen, Germany, cholera derived from the diffusion of 1865, seemed to have ceased in Europe, as I have already related, in 1868. When the next year, 1869, early in August, the disease appeared in the city of Kiev, it was not at first recognised as the epidemic malady. So completely had the previous prevalence of cholera in the Empire seemed to have come to an end, that the likelihood of a recurrence did not occur to any observer, until the spread of the disease in the city and to neighbouring governments showed its true nature.

The following account of the outbreak at Kiev in 1869 is given by Dr. Pelikan, the director of the Medical Department of the Russian Government:—*

"In 1869 cases of cholera began to appear at Kiev from the spring, namely, from May $\frac{16}{28}$, when a private of the 46th Dnieper regiment, Matthew Sopchuk, was attacked by the disease in camp; on June $\frac{17}{29}$ Michael Michaelson, a regimental servant belonging to the Kiev artillery, was seized with it; and on July $\frac{13}{25}$ a woman of Kiev, called Ardotia Vitughina, was similarly attacked. Between July $\frac{19}{31}$ and August $\frac{1}{13}$ two gunsmiths, who had arrived at Kiev from the Ijef works in the province of Viatka, and two women belonging to the family of another gunsmith called Lusiatnikoff, likewise from the province of Viatka, were attacked by cholera; and on August $\frac{8}{20}$ a woman from Briansk, who had come to Kiev on a pilgrimage, took the disease. All these cases terminated fatally, either on the same day or on the next, with all the symptoms of Asiatic cholera. From August $\frac{12}{24}$ cases of cholera began to occur daily at Kiev, but as they were confined exclusively to persons who lived under sanitary conditions so unfavourable as to be sufficient of themselves to produce sporadic cholera, the epidemical character of the disease was not defined until after it had attacked consecutively several persons who enjoyed the benefit of living under good sanitary conditions. It must, however, be observed that the cholera epidemic was extremely inconsiderable at Kiev, notwithstanding the immense concourse of pilgrims from the various provinces of Russia, and notwithstanding also that the pilgrims were subjected to the worst possible sanitary conditions. The total number of persons who were attacked by cholera at Kiev in 1869 was 263, while the number of deaths was 152. Such a feeble diffusion of the epidemic, under circumstances apparently so favourable to its retention, caused many Russian medical men to consider the prevalent disease to be not Asiatic cholera ('*cholera Asiatica s. epidemica*') but European cholera ('*cholera nostras*'). But the onward movement of the disease, and its consecutive appearance in the town of Orel (where, from November $\frac{3}{15}$ to January $\frac{15}{27}$, 1870, the number of cholera cases was 407, and that of deaths 224), and later in the winter of 1870 at Moscow very clearly showed its character, and proved that the medical men of Kiev had been right when they pronounced the disease to be Asiatic cholera. In other localities the cholera occurred either in small groups of cases and of mortality or in entirely isolated cases, so that, inclusive of the epidemics in the provinces of Kiev and Orel, the total number of cases of cholera in Russia in the year 1869 was barely 911, and that of deaths 510."

Dr. Arkhangelsky's account of the outbreak at Kiev corresponds with that of Dr. Pelikan in respect to the early cases of the disease in the city, but differs somewhat as to the total sickness and mortality from it, not only there, but also in European Russia generally, this year. According to Dr. Arkhangelsky, 338 cases of cholera occurred at Kiev, of which 162 died, the outbreak commencing on the $\frac{8}{20}$th August and ending on the $\frac{3}{15}$ December. The disease next appeared in the Government of Minsk, when 33 cases were recorded and 26 deaths, from the $\frac{23\text{ October}}{4\text{ November}}$ to the $\frac{26\text{ December 1869}}{7\text{ January 1870}}$. It then showed itself in succession in the Governments of Tula ($\frac{1}{13}$ November), Orel ($\frac{3}{15}$ November), Poltava $\frac{12}{24}$ November), Kursk ($\frac{27\text{ November}}{9\text{ December}}$), Smolensk ($\frac{2}{14}$ December), Moscow ($\frac{25\text{ December 1869}}{6\text{ January 1870}}$). Cases also occurred in the Governments of Kaluga, Novgorod, and St. Petersburg, but the dates of occurrence are not given.

* Memorandum communicated through the Foreign Office to the Medical Department of the Local Government Board, 1873.

In the greater number of the governments the outbreaks continued into the following year (1870), in Tula uninterruptedly until November, but in the other governments ending in the early months to re-appear again at a later date. The governments which suffered most in addition to Kiev were Moscow and Orel. In the former government, 261 cases and 122 deaths were recorded from the $\frac{25 \text{ December } 1869}{6 \text{ January } 1870}$ to the $\frac{27 \text{ April } 1870}{9 \text{ May } 1870}$; in the latter government, 502 cases and 293 deaths, from the $\frac{3}{15}$ November 1869 to the $\frac{5}{17}$ March 1870. The total number of cases of cholera which occurred in European Russia from the $\frac{8}{20}$ August 1869 to the $\frac{5}{17}$ 5th March 1870 (the return for Tula being given to the $\frac{1}{13}$ January) was, according to Dr. Arkhangelsky, 1,276, of which cases 659 died. (*See* Map 1869.)

Eleven governments of European Russia were infected with cholera in 1869. The following year, 1870, the infection spread over 37 governments, including five of the governments of Poland. The disease did not reappear either in Kiev, or Poltava, or Minsk this year, and it was distributed mainly in the eastern provinces of the empire. I quote Dr. Arkhangelsky's account of the appearance and spread of the disease in 1870 :—

" The existence of cholera again in Central Russia, in 1869, had become indisputable. In the winter of 1869–70 the action of this agent was observed in the government of Orel to the $\frac{5}{17}$ March, in the government of Moscow to the end of April, and in that of Tula until summer, when the disease began to spread rapidly. The epidemic character of the disease first showed itself [this year] in the government of Ekaterinoslav-with-Taganrog. The person earliest attacked was a peasant from the government of Orel who had gone to Taganrog to labour in the fields. He was admitted into the hospital of the Charitable Institutions, on the $\frac{1}{13}$ June, suffering from a severe seizure of cholera, precursory symptoms having showed themselves on the $\frac{30 \text{ May}}{11 \text{ June}}$. At the time of his admission the sanitary state of the hospital was very bad, and next day cholera began to spread among the patients and attendants, afterwards extending into the town. In the government of Orel cholera was first officially recognised this year on the $\frac{1}{13}$ July. The circumstances under which the disease appeared there remain unexplained. Most likely there were isolated cases at an earlier date which escaped the attention of the medical men. The particulars of the dissemination of the epidemic in 1870 are given in the Epidemiological section of the ' Journal of Forensic Medicine and Social Hygiéne ' for the year. The railways between Taganrog and Moscow, and between the Volga and the Don, performed generally a prominent part in the dissemination of the disease ; but notwithstanding the considerable net-work of railway communications and the great extension of steam-navigation on the rivers, cholera spread itself very gradually as may be seen from the table. [See *Appendix*, Table XI.]

" The total length of railway routes in Russia amounted, in 1870, to 10,531 versts, whereas in 1866 the amount hardly reached 4,351 versts, that is to say, there had been an increase of 6,180 versts during the four years. From the Table [XI.] it will be observed that in addition to the governments of Tula, Orel, and Ekaterinoslav, cholera appeared in July [O.S.], in those of Taurida ($\frac{7}{19}$), Kherson ($\frac{21 \text{ July}}{1 \text{ August}}$), Kharkoff ($\frac{28 \text{ July}}{9 \text{ August}}$), also in the district of the Don Army ($\frac{27 \text{ July}}{8 \text{ August}}$), and the government adjacent to it, the district of Kuban [Cis-Caucasia] ($\frac{27 \text{ July}}{8 \text{ August}}$), in the governments of Saratov and Simbirsk ($\frac{29 \text{ July}}{10 \text{ August}}$), the government adjacent

to Orel, namely, Kursk ($\frac{19}{31}$), and in Voronej ($\frac{24\text{ July}}{5\text{ August}}$). In August [O.S.], cholera appeared on the shores of the Black Sea, and on the northern slope of the Caucasus ($\frac{4}{16}$), in the government of Stavropol ($\frac{15}{27}$), Astrakhan ($\frac{14}{26}$), Samara ($\frac{15}{27}$), Kazan ($\frac{19}{31}$), Nijnigorod ($\frac{18}{30}$), Pensa ($\frac{22\text{ August}}{3\text{ September}}$), Vladimir ($\frac{24\text{ August}}{5\text{ September}}$), Moscow ($\frac{25\text{ August}}{6\text{ September}}$), Kaluga ($\frac{8}{20}$); and, to the north-east, Perm ($\frac{24\text{ August}}{5\text{ September}}$), Viatka ($\frac{31\text{ August}}{13\text{ September}}$), and Kostroma (date undetermined). To the north-west cholera appeared the same month (August [O.S.]) in the governments of St. Petersburg ($\frac{16}{28}$), Olonetz ($\frac{24\text{ August}}{5\text{ September}}$), and Novgorod ($\frac{28\text{ August}}{8\text{ September}}$). The governments in which the epidemic appeared in September [O.S.] were Tambov ($\frac{13}{25}$), Jaroslav ($\frac{7}{19}$), and Orenburg ($\frac{8}{20}$); in October [O.S.], Grodno ($\frac{28\text{ August}}{9\text{ September}}$), Warsaw ($\frac{2}{14}$), and Radom ($\frac{11}{23}$); and in November [O.S.], Wilna ($\frac{1}{13}$), Kovno ($\frac{30\text{ November}}{12\text{ December}}$), Kalisch ($\frac{2}{14}$), Plock ($\frac{16}{28}$), and Petrokov ($\frac{14}{26}$).

"The epidemic intensity was in general weak, the mortality scarcely exceeding 1 per 1,000 of population. In the government of Orel it was 1·3; in the district of the Don Army, 1·1; and in the government of Ekaterinoslav-with-Taganrog, 1·0. In the remaining governments the mortality per 1,000 population was under 1. Cholera did not appear in the government of Riazan, notwithstanding that the governments surrounding it were infected, and that it was in communication by railway with Moscow. This railway, 196 versts in lengths, carried upwards of 660,000 passengers in 1870, a number little less than that carried by the Kursk-Kharkov railway, 736 versts in length, namely, 736,000. If the different length of the lines be considered, the traffic must have been greatest on the Tambov line. Moreover, on this line there are four intermediate stations."

The geographical distribution of the governments in the order of their infection, in 1870, from the beginning of the epidemic activity in Taganrog, is noteworthy. Taurida, Kherson, Kharkov, the country of the Don Cossacks, and the district of Kuban surround Ekaterinoslav-with-Taganrog—Taganrog, Taurida, and Kuban, lying largely in the basin of the Sea of Azov, and the country of the Don Cossacks in the valley of the Don, where, by reason of the railway between Kalatch and Tzaratzin, the valley becomes part of the commercial system of the Volga. Simbirsk and Saratov lie on the west bank of the Volga, Astrakan on the lower waters, Samara on its left bank, Kazan, Nijni-Novgorod, Vladimir, and Kostroma on the upper waters, Novgorod and Olonetz on its main northern and western affluents, and Perm and Viatka on its main northern and eastern affluents. The peculiarities of geographical distribution here noted, are not without significance in relation to the question of the source of that recurrence of epidemic cholera in European Russia, which is now under consideration.

The total number of cases of cholera recorded in European Russia in 1870 was 21,663, of deaths, 9,386. In Poland the cases numbered 524, the deaths 218. (See *Appendix*, Tables XI. and XII.)

Dr. Arkhangelsky makes no further reference to cholera in Caucassia in 1870 than those which have been quoted with regard to its appearance in the district of Kuban in July, and on the Caucasian coast of the Black Sea, and in the government of Stavropol in August. According to official information, communicated to this Department, the disease appeared at Poti about the $\frac{1}{13}$th August, and prevailed there more or less until the beginning of October. Extending up the valley of the river it broke out at Kutais and Tiflis, in both places, about the $\frac{15}{27}$th August, prevailing there until November; and in September it was

reported to be present at Nakitchivan, and other places on the Persian frontier. (*See* Map VII.)

It is not necessary to follow in any lengthened detail the progress of cholera in Russia in subsequent years. The Tables appended (Tables XIII.–XIX.) give the particulars as to times of appearance, duration of prevalence, sickness and loss of life from the disease, during the years 1871, 1872, and 1873. Here I propose to describe briefly the general distribution of cholera in the Empire during the period in question, and such dissemination and development as occurred beyond the limits of Russia. (*See* Maps V.–X.)

Russia, 1871.

In 1871 cholera was generally diffused throughout Russia in Europe. The disease extended from the north coasts of the Black Sea and the Sea of Azov in the south, to the south coast of the White Sea (Archangel) in the north, and from the Prussian frontier and Baltic coast in the west to the Ural mountains in the east. It spread also into Western Siberia, appearing in the government of Tobolsk on the $\frac{31 \text{ July}}{12 \text{ August}}$. It was reported also, to this Department, as having prevailed along the course of the Kuban in Caucasia, and as having appeared in Transcaucasia at Baku and Erivan. During the prevalence of cholera in European Russia this year it attacked 322,711 persons, and killed 124,881; in Poland it attacked 4,959, and killed 1,685 ; and in Western Siberia it attacked 1,130, and killed 371. The total seizures from the disease ascertained in the Empire this year were 328,800, the total deaths 126,937. (Tables XIII., XIV., XV.)

Prussia, 1871.

On the 13th July cholera passed the Prussian frontier in the government of Gumbinnen, on the route to Königsberg, "the chief northern outlet of the Russian Empire,"* where the disease broke out on the 24th of the month. A week later it appeared at Hamburg and Altona. Cholera underwent considerable development in several districts of the kingdom, the total number of attacks from the 13th July to the 8th November being 6,961, the total number of deaths 3,841. The disease was most severe in the government of Königsberg, where it prevailed from the 24th July to the 8th November, causing 3,868 seizures and 2,012 deaths. In Hamburg, from the 1st August to the 24th September, there were 171 cases and 101 deaths.†

* Mr. Rumbold, H.M. Secretary of Embassy, St. Petersburg.—*Commercial Reports*, 1871, p. 101.

† Cholera.—Prussia, 1871.

Districts.	Duration of Outbreak.		Cases.	Deaths.
	Beginning.	End.		
Gumbinnen - -	13 July	?	1,766	958
Königsberg - -	24 ,,	8 Nov.	3,868	2,012
Dantzig - - -	1 Aug.	7 Oct.	272	181
Marienwerder - -	21 ,,	7 Nov.	127	89
Berlin (city) - -	14 ,	14 Oct.	67	52
Potsdam - - -	20	25 ,,	116	71
Frankfort - -	29 ,,	21 ,,	74	61
Stettin - - -	11 ,,	21 ,,	383	212
Posen - - -	19 ,,	26 ,,	150	84
Schleswig-Holstein -	21 ,,	1 ,,	166	106
Lüneburg and town -	4 Sept.	2 Nov.	20	13
Merseburg - -	9 ,,	2 ,,	2	2

Sweden, 1871.

Further north, the disease appeared in August at Helsingfors, in Finland, where, until its cessation on the 18th October, there were 300 cases and 165 deaths. It extended also to the opposite coast of the Baltic, at Hernosand, causing there from the 10th September to the 22nd, 18 cases and 11 deaths. Gothenburg also and the neighbouring district were attacked, about the same time apparently, and 35 cases of cholera were recorded, of which 21 were fatal.

Extension to North America 1871.

On the 10th October an ill-furnished emigrant steam-ship sailed from Stettin, where cholera then was, for New York, touching at Copenhagen and Christiansand. About a week after this vessel had left Christiansand cholera appeared among the passengers, 610 in number. She put into Halifax, Nova Scotia, and introduced cholera into that city, and into the village of Chezet-cook, 25 miles north of Halifax.*

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* The following is a report of this introduction of cholera into Nova Scotia, by Dr. L. M. V. Lloyd, Deputy Inspector-General of Hospitals, communicated, by the Director-General of the Army Medical Department, to the *Lancet*, 17th February 1872, p. 226 :—"Chezet-cook is a small fishing village on the south-east coast of "Nova Scotia, and about 22 miles from Halifax; the inhabitants are French "Acadians. The steamship 'Franklyn' (Captain Dyer) left Stettin on the 10th of "October, Copenhagen on the 12th, and Christiansand on the 15th of the same "month (which ports were reported to have been then healthy), bound for New "York, with some 600 German emigrants on board. She left with an insufficient "supply of water and coal, especially of the former, and had a very stormy passage. "On October 23rd, eight days after leaving Christiansand, the first death occurred, "date of first appearance of sickness not ascertained. Previous to the occurrence of "any sickness the water failed, and was supplied to the cabin passengers only, those in "the steerage having condensed water for cooking and drinking, and this was "brackish from the coil of the condenser being out of order. The emigrants were "confined below decks during the stormy weather. The vessel reached Halifax on "November 6th, 22 days from last port, and 14 days after first fatal case, short of "coal and water. Having had fresh supplies, she proceeded, after a short delay, to "New York, before anything was known of her sickly condition; and it was only "after her arrival at that port that we learned she had some 40 deaths previous "to calling here. There are various reports as to the statements made by the "captain to the health officer; they were, however, such as to deceive him, and to "warrant his permitting the ship to have communication with the town, for which "he is now under suspension pending the result of an inquiry by order of the "Dominion Government. I have not been able to learn whether the emigrants "had come from infected localities; and as to the condition of the vessel, all I can "ascertain is that she was 'comparatively clean.' On the day of her arrival (the 6th) "a named Melvin went on board to supply her with water, and was similarly "employed on the 7th; and went below decks to turn on the tap. He had pre-"viously been suffering from diarrhœa; was seized on the 13th of November with "symptoms of Asiatic cholera, and died on the 14th, after 12 hours' illness. His "medical attendants at once pronounced the disease to be cholera and every pre-"caution was rigidly enforced; his clothes and bedding were burnt, and the house "thoroughly fumigated. No other case occurred. The disease was brought to "Chezet-cook by Dennis Lepiere, who had been employed coaling the steamer on "the 7th November; he stood several hours on the gangway leading from the "vessel supplying the coal, and was engaged shovelling it into the steamer. It is "rumoured he got drunk, and was placed below decks of the steamer until sober; "but this is uncertain. On the 13th of November he was seized with severe "purging, vomiting, &c., and was driven in a cab to his father's house at Chezet-"cook. The symptoms became worse after his arrival—cramps very severe, "intense thirst, extremities very cold and blue, &c.; but he recovered slowly, and "in a few days could move about. On the 17th of November Mary Lepiere, "aged 34, who lived about a quarter of a mile from her cousin Dennis Lepiere, on "whom she attended for a night, was seized with symptoms similar to his, but more "severe; cramps extremely severe, eyes turned up and sunken, hands livid, face "and lips blue, &c. On the 18th she died after 20 hours' illness. On the 18th "November Margaret Lepiere, aged 21, a strong healthy women, sister to Dennis "(No. 1), with whom she lived, was seized with similar symptoms, which were also "very severe, but from which she ultimately recovered. In this case there was "suppression of urine for four days. Bridget Lepiere, aged 40, married women,

On the opposite side of the Continent cholera was more widely scattered beyond the limits of Europe in the course of the year.

In September the disease broke out at Constantinople. Isolated cases were reported on the 20th of the month, and from the 26th September to the 24th December 3,158 deaths occurred.

In the course of October and November cholera appeared at several places on the Danube. On the 17th October the disease was present at Sulina, and in November 26 deaths were recorded at Tultcha. Galatz also was infected. At the beginning of November 10 cases and six deaths occurred at Samsun, on the southern coast of the Black Sea, and in the third week cases occurred at Trebizond. The same week also several cases occurred at Varna.

South of Constantinople three cases of cholera, of which one was fatal, took place on the 10th November in the lazaretto at Salonika ; and the following month the disease appeared at a village 12 miles distant from that town, following upon the return of persons from Constantinople, who had been detained in quarantine. At St. Jean d'Acre an outbreak occurred, of which the first case was a traveller coming from Constantinople, landed ill of cholera from a passenger steamer.

" previously in good health, was seized on the 19th November with symptoms of a " very severe nature. She had been attending the others, and had 'laid out' the " body of Mary Lepiere (No. 2) on the evening previous. She died on the 21st, " about midday. Her symptoms were so severe, and the panic so great, that her " body was abandoned before her death even by her husband. Sarah Lepiere was " attacked on the same day as her sister Margaret, namely, on the 18th. She lived " in the same house, was only five years of age, and, although severe, the case " recovered. The symptoms were nearly the same in all the cases: cramps very " severe, vomiting and purging of 'rice-water stools,' patients absolutely pulseless, " eyes turned up and sunk in the socket, upper lip contracted, the 'risus sardonicus,' " intense thirst, face swollen, lips blue, and arms blue from elbows to the tips of " the nails; and one case, No. 3, had suppression of urine for four days. No sectio " cadaveris was made. After death the legs and thighs were flexed to an extreme " degree, face swollen and blue, nose pinched, upper lip retracted, arms blue, hands " clenched, &c. The rigor mortis was so extreme that the coffin had to be made to " adapt itself to the curvatures of the body. No medicines were of any avail, as " the stomach rejected everything. Very weak brandy and water, administered " frequently in small doses, seemed to be most useful. The suppression of urine in " case No. 3 was overcome apparently by hot baths. The disease did not extend " beyond the Lepiere family, I believe, owing to the very energetic manner in which " all needful sanitary measures were enforced. Drs. Jennings and Rigby on being " sent down by the Government enforced the strictest quarantine. Sentries were " placed on every road at the distance of five miles from the village, not even the " mails being allowed to pass, and ships were not allowed to approach the coast. " The dejections from the patients were received into vessels in which were placed " carbolic acid, chloride of lime, &c., and were covered with these and with earth " before being buried. The infected houses were also quarantined from the rest of " the village. The bedding, clothing, &c., were all burned; and the furniture, " houses, &c., thoroughly disinfected and scrubbed. For the facts embodied in this " report I am indebted to the health officer of the port, and to the medical gentle- " men in attendance on the sick. No case of Asiatic cholera had appeared in " Halifax since the spring of 1866, when the steamship 'England' arrived in a " sickly condition, and suffered severely. That the disease was imported by the " 'Franklyn' there can be no doubt. Some of the passengers most probably came " from an infected district; and all were placed under the most unfavourable con- " ditions, using brackish water, and being confined below in bad weather, conditions " predisposing to, and favouring the spread of, the disease. The men Melvin and " Lepiere, employed at the same time in coaling and watering, were exposed for " some hours to the poisoned air on board of, or escaping from, a ship in which " some 40 deaths had occurred during the previous fortnight, and both took ill the " same day; one case proving fatal in 12 hours, and the other communicating the " disease to members of his family, all which facts, it must be admitted, clearly " prove the propagation of the disease by infection."

In November also the disease appeared at Ismid (Nicomedia), on the Asiatic coast of the Sea of Marmora.

1871, *Anatolia.*

But before cholera had appeared at Constantinople, and before there had been any extension of the disease beyond the limits of European Russia, the disease seems to have been present in parts of Asia Minor. At the commencement of August cholera broke out at Brusa, in Anatolia, in succession to appearances of the disease in villages south of the city. These appearances are believed to have begun in June at Harmandjik, a town 36 hours south-east of Brusa. Late in November the disease was reported to be present at Kutaya, 80 miles to the south-east of Brusa, and in December it appeared at Amassia, and in Roum. The latter outbreak may have been connected with the introduction of cholera into Samsun the previous month; but at the time of the believed appearance of cholera in the district between Brusa and Kutaya, cholera is not known to have been prevalent nearer to this locality than Southern Russia or the north of Turkish Kurdistan.

1872, *Russia.*

In the year 1872 cholera was almost as widely spread in European Russia as in the previous year. In 1871 the disease was prevalent in 49 governments, in 1872 in 46. Bessarabia, which escaped the epidemic the former year, suffered in 1872; while Archangel, Vologda, Courland, and Livonia, which were then infected, now were free from the malady. The seizures during the year were 310,607, the deaths 113,196, as compared with 322,711 and 124,831 in the previous year. Poland, of which four of the governments had suffered from the epidemic in 1871, had the disease prevalent in eight in 1872. In the latter year the seizures in this kingdom were 12,033 [? 15,749], and the deaths 5,280 [? 5,597]; in the former year the seizures had been 1,130 and the deaths 371. (See *Appendix*, Tables XVI. and XVII.)

1872, *Austria.*

This year cholera invaded Central Europe from Russia through Galicia. To the westwards there seems to have been a slight scattering of the disease only. It reappeared at Helsingfors in July; and a group of eight cases, six of which were fatal, occurred at Gefle, on the Swedish coast, between the 28th August and the 9th September. Two cases also, one of which was fatal, occurred at certain ironworks a mile from this port. In East Prussia and Prussian Silesia there was a scattering of cases from infection across the Polish frontier. On the eastern extremity of the Russian frontier cholera passed into Rumania, spreading over several districts of Moldavia. During this prevalence in Rumania 1,093 attacks were recorded, of which 524 died. (See *Appendix*, Table IV.)

Cholera entered Galicia on the 29th May 1872, and spread over that province and the Bukovina, extending westwards into Moravia and Bohemia, and southwards throughout Hungary. With the exception of the Bukovina the disease continued active in these provinces until late in the following year (1873). The official summary returns do not separate the sickness and loss of life of the two years, and these will be given in the account for 1873. In the Bukovina, cholera appeared on the 3rd August and ceased on the 28th November. Within this period there were 1,689 cases of the disease, of which 724 died.

1873, *Russia*

In 1873 cholera reappeared in 14 governments only of European Russia; but in Poland and Central Europe the disease increased in intensity, and it now spread over a considerable portion of Western, and some parts of Southern Europe.

The number of cases of cholera in European Russia this year was 9,847, the number of deaths from the disease 4,395. The number of cases in Poland was 63,491, the number of deaths 29,733. The disease in European Russia prevailed most in the governments of Volhynia, Grodno, and St. Petersburgh; in Poland in the governments of Warsaw, Keletz (where the mortality was 11·3 per 1,000 of population), Lublin, Petrokov, and Sedletz.

The sickness and loss of life in Austria and number of localities in which it prevailed is shown in the following table:—

Austria, 1872–1873.

Austria, 1872–73.

Provinces.	Duration of Outbreak.		Number of Localities attacked.	Population.	Cholera.	
	Beginning.	End.			Cases.	Deaths.
Galicia - -	29 May 1872.	31 Sept. 1873.	3,611	4,098,319	243,680	94,766
Bohemia -	28 Nov. 1872.	31 Aug. 1873.	110	363,915	6,532	3,588
Moravia -	3 „	30 Sept. 1873.	119	249,695	3,140	1,488
Silesia - -	28 „	20 Aug. 1873.	81	85,790	1,594	647
Lower Austria	4 April 1872.	29 Nov. 1873.	164	424,247	6,533	3,232
			4,085	5,221,966	261,479	103,721

In Vienna, (population 657,100,) from 4th January to the middle of November (the epidemic extension commencing in July), the number of cases of cholera registered was 2,854, of deaths from the disease, 2,123.

Hungary, 1873.

Hungary suffered to a greater extent from this invasion of cholera than Austria. From September 1872 to December 1873, there were attacked by the disease in this division of the Austrian Empire, 6,507, towns and villages, and in 231 of these places cholera had not wholly ceased when the year 1873 came to an end. Within this period, among a population stated to number 8,675,517, there were 443,641 cases of cholera, of which 187,407 were fatal. In Buda-Pesth, from the 18th October 1872 to 15th October 1873, there were 6,705 cases of cholera, and 3,159 deaths from the disease.

Austro-Hungary was the principal seat of prevalence of cholera in Central Europe in 1872, as it was in 1873. From this area of prevalence, and from the Polish frontier, the disease radiated more or less in all directions eastwards, southwards, and westwards. Passing along the valley of the Danube from Hungary, it attacked the principal towns on both banks of the stream, (Widin, Rustchuk, Silistria, Braila, and Galatz,) and spread into the districts on both sides. On the Rumanian side, within the Principalities, it attacked 11,516 [? 11,696] persons, and killed 3,864 [? 3,845]. (*See* Appendix, Table V.) On the Bulgarian side no proper records of its extension, and of the sickness and mortality arising from it, were kept. The disease appeared at Rustchuk during the first week of June, where it was most severe among the

Rumania, 1873.

Turkey, 1873.

troops stationed there. Subsequently it broke out in a large camp of exercise at Shumla, south-east of Rustchuk, in the interior, and afterwards in the town and neighbouring villages. According to the imperfect and untrustworthy records kept, there were 315 deaths from cholera among the troops, 407 deaths among the civil population of the town, and 521 deaths in neighbouring villages. Cholera was also conveyed into other parts of the interior, and appeared at Sophia, and in August in two or three localities of the vicinity of Salonika, to which it seems to have been propagated from the interior.

On the Bosphorus, in the lazaret at the northern entrance, several cases of cholera were received from ships arriving from ports on the Danube, and the disease was propagated to some of the guards and attendants. Two soldiers, moreover, were attacked with cholera in Constantinople immediately after being freed from quarantine, but the cases were sterile.

1873, *Southern Austria.*

South of Hungary, where cholera had been prevalent, on the right bank of the Save, along the Austrian military frontier, the disease ascended the valley of the Unna, attacking Dubitza at the foot, and Bihacs at the head, killing altogether about 1,000 persons. West of Bosnia, the Austrian ports of Trieste and Fiume both suffered from the epidemic, the former from the 13th August to the 20th November, having 620 cases and 353 deaths among a population of 120,000. Further west cholera crossed the Venetian frontier from Hungary into Italy, and from Venetia it passed into Lombardy and Parma, and reaching Genoa in August was propagated to Naples in September. In Venice, cholera appeared on the 24th June, and lasted until 10th October, during which period there were 800 cases and 459 deaths. Elsewhere in Italy, except in Naples, so far as my information extends, the local outbreaks were few in number and not of much magnitude.*

The westward extension of cholera this year included Prussia, Saxony, Bavaria, Wurtemburgh, North-western France, and to some extent Belgium and the Netherlands.

1873, *Prussia.*

In Prussia not less than 23,242 lives were sacrificed by the disease in 1873, out of 45,589 persons attacked.† In the kingdom of Saxony there

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* I have not been able to obtain any general report for this year, such as the reports published relating to the diffusion of cholera in 1865–67 in Italy, and have even been foiled in my attempts to ascertain whether such a report has been printed by the Italian Government.

† Cholera.—Prussia, 1873.

	Cases.	Deaths.
Province of Prussia - -	25,261	13,268
„ Brandenburg - -	3,594	1,721
„ Pomerania - -	529	351
„ Posen - - -	1,429	776
„ Silesia - - -	3,667	1,773
„ Saxony - -	10,246	4,834
„ Schleswig-Holstein -	228	156
„ Hanover - -	578	346
„ Hesse-Nassau - -	57	17
	45,589	23,242

(Quoted from the *Staats Anzeiger* in the *Gazette Hebdomadaire de la Médécine et de Chirurgie* for the 2nd January 1874.)

were 766 cases of cholera and 361 deaths from the disease.* Cholera appeared in Munich on the 25th June, and during the six following months (the outbreak continuing into 1874), there were 2,027 cases of the disease in the city, of which 934 were fatal. Other towns in Bavaria did not entirely escape from the epidemic. In Wurtemburg the disease showed itself at Heilbronn, and in few neighbouring places, the total attacks amounting to 168, the total deaths to 78. The extent of prevalence of the disease in France is very imperfectly known. No official account of the extension there has been published, and the Report of the Academy of Medicine on the epidemics of this year has not yet appeared. According to a report, by Dr. Denis Dumont, on cholera in the department of Le Calvados, the disease appeared there this year in the Commune of Bretteville-sur-Lame on the 15th July, causing from that date to the 5th August 30 deaths. Other Communes in the Department suffered slightly, Ifs, (7 deaths), Gayelles, Oyestreham, (18 deaths), Bretteville-sur-Oder, (9 deaths). The disease appeared in Caen on the 24th August, and from that date to the 8th November it is estimated that there were 1,086 cases, and 497 deaths.† In July, also, a fatal case of Asiatic cholera was reported on an English vessel at Rouen, and soon after the disease was reported to have broken out in Havre. The presence of cholera in this port was not officially recognised until some time afterwards. The disease continued here until the 11th December but no complete account of the sickness and mortality has been published. Cholera appeared in Paris on the 5th September, and continued there three months, causing 855 deaths.

Bavaria, 1873.

Wurtemberg, 1873.

France, 1873.

In Belgium cholera appeared at Antwerp on the 20th September, and caused in the three following months 135 cases and 86 deaths. There was a scattering of the disease in several provinces of the Netherlands, but no serious prevalence. Hamburg suffered from a sharp outbreak, which, beginning on the 21st June and ending on the 8th November, attacked 1,483 persons, killing 1,002. Denmark escaped from the diffusion, although cases were imported into Copenhagen. Eleven deaths from cholera were reported in Lubeck. On the eastern side of the Sound, in Sweden, 561 cases of cholera, of which 275 were fatal, occurred in the district of Helsingborg and parishes of Höganas and Wäsby. Further north, in Norway, there were 20 cases of cholera and 10 deaths from the disease in Bergen and the neighbourhood, during August and September. Still further to the north, in the district of Helsingfors, Finland, eight cases of cholera, five fatal, were reported at Joensun.

Belgium, 1873.

During this prevalence of cholera in Western Europe, England did not escape numerous importations of the disease, all of which proved sterile. In July several cases were imported into London and the Thames from Rotterdam. In September cases were imported into the Thames, into London, and into the ports of Southampton and Swansea from France. In October a case was imported into London direct from Prague, and

England, 1873.

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* Cholera.—Kingdom of Saxony, 1873.

Government.	Cases.	Deaths.
Dresden - -	683	322
Bautzen - -	22	11
Leipzig - -	37	25
Zwickau - -	4	3
	766	361

In the city of Dresden the cases numbered 156; the deaths 99.

† Rapport sur l'Epidèmie Cholérique de 1873 dans le Calvados. Par le Dr. Denis-Dumont Caen, 1874.

END OF THE DIFFUSION BEGINNING IN 1865.

the same month several cases were imported from Havre into Liverpool, some by way of Southampton and thence through London by rail to Liverpool, others by ship direct into the Mersey.*

When the year 1873 came to a close cholera still existed in Russia, in the Governments of Grodno and Mohilev; in the Netherlands, at Rotterdam ; and in Munich. In Russia the disease became extinct in January 1874, the latest cases being reported in the Government of Mohilev. Eleven cases of cholera, six fatal, were reported in Rotterdam from the 1st to the 21st January 1874. On the 1st April a fatal case was also reported, since which date the disease appears to have ceased in that port. In Munich cholera had continued throughout the winter and into the spring of 1874. During its prevalence in the city, this year, the seizures were 1,016, the deaths 526, making from the commencement of the outbreak in June 1873, to its close in April 1874, the total number of attacks 3,040 and of deaths 3,060, among an estimated population of 170,000. In February, 1874, cholera was active in several localities of Prussian Silesia. Fifty deaths were reported, early in April, to have occurred in this province. On the 9th July the *Journal de St. Petersbourg* quoted a statement, from the Russian Academy Gazette, that cholera had broken out in several places in Poland. Dr. Arkhangelsky, in his observations on the prevalence of cholera in European Russia in 1873, and the extinction of the disease in that country at the beginning of 1874, makes no reference to Poland.

Of the further progress of cholera in Prussian Silesia and Poland in 1874 I know nothing, and such inquiry as it has been possible for me to

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* The following facts, relating to the spread of cholera in Europe in 1873, illustrate the difficulties attending the imposition of an effective quarantine, and the necessary failure of quarantine restrictions where active and rapid communication is maintained between countries. The first intimation of the eastward movement of cholera in Europe in that year (cholera having been present throughout the whole of the winter of 1872–73 in parts of Austrian Silesia, Bohemia, and Hungary) was given in a telegram from Her Majesty's Representative at Constantinople, dated the 10th May 1873, and which conveyed the information of the presence of cholera in Widdin, the establishment of a *cordon sanitairè* there, and the imposition by the Ottoman Board of Health of quarantine on arrivals from the Upper Danube. Subsequent communications from Constantinople showed that 34 cases of cholera, 15 ending fatally, had occurred in Widdin between the 26th April and the 12th May 1873, and that the disease had prevailed at Lom (Bulgaria), beginning in February and ending at the close of April.

The first intimation of the westward movement of cholera in Europe, the same year, was contained in a telegram from Gumbinnen, East Prussia, published in the *Times* of the 4th June, and which announced the appearance of the disease in two villages of West Prussia. The first official intimation of the movement of cholera westward was forwarded from Danzig, by Her Majesty's consul there, on the 5th June. The despatch recorded the appearance of cholera among raftsmen of the Vistula, in that portion of the navigation which lies between the mouth of the Vistula and the entrance to the canal leading to Danzig. Cholera first appeared in West Prussia on the Vistula, in the government of Marienwerder, on the 26th May.

The first intimation of the presence of cholera in St. Petersburg was received on the 9th September, the disease having appeared there on the 10th August. Cholera was officially recognized in Havre on the 2nd September, the disease having been present there since the 9th August, and after a formal contradiction of the reported presence of the disease on the 29th August. The first intimation of cholera in Hamburg was received on the 1st August, after inquiry made from this country, in consequence of several cases of cholera having been landed at Blackwall, from a ship which had sailed from Hamburg on the 26th July. Cholera had been present in that port since the 21st June. Information was received of cholera in Rotterdam on the 18th October, but its existence there was not officially declared by the local authorities until the 27th October. Information was received of the presence of cholera in Antwerp on the 25th October, but at that date clean bills of health were still being issued to ships leaving the port.

make has failed to the present in eliciting information on the subject. Presumably, having regard to the sources of information which were accessible in 1874, notably during the meetings of the International Sanitary Conference at Vienna that year, the disease died out in Prussian Silesia and Poland before the year came to an end. Practically, so far as the epidemic diffusion is concerned, of which these later manifestations were the fag end, such was the case. (*See* Maps V.–X.)

§

Observations on the Origin of the Recurrence of Cholera in Europe in 1869.

The recurrence of cholera in Europe, beginning in 1869 and ending in 1874, which I have described, was one of a series of phenomena of like character.

In 1868, as already related (p. 108), after a general movement from westward to eastward in Persia, and during a period of declining prevalence, cholera became exceedingly active in that country. Breaking out at Meshed, also at a time of pilgrimage, the disease soon spread from this city, as a centre, once more over the country, returning upon the steps of the previous diffusion, so to speak, and passing at more than one point beyond the limits of Persian territory.

Preceding this recurrence of cholera in Persia, there had been the previous year (1867) a great extension of cholera in Northern India and Afghanistan. In 1865–66 the North-western provinces were newly invaded by migrating cholera from the Lower Provinces, and in the latter year the invasion included the Southern Punjab. In 1867 the invasion extended throughout the Punjab and into Eastern Afghanistan. The great Hindoo religious fair at Hurdwar, on the Upper Ganges, where the river issues from the mountains, exercised an important influence upon the diffusion of cholera in Northern India this year. The fair was held in April, and it is estimated that the extraordinary number of 2,800,000 persons were present on the principal day of the religious rites. At the close of the fair, cholera broke out among the assembled multitude as they were about to disperse, and it clung to the different bodies returning homewards, and was disseminated by them along the different routes they travelled. In July 1867, cholera broke out in Cabul, and prevailed in that city with such intensity that not less than 8,000 lives are estimated to have been lost from the disease in the period of a month or thereabouts. The disease extended to the country surrounding Cabul, the villages there suffering from it proportionately to as great an extent as the city. Towards the close of August, cholera had considerably decreased in Cabul, and business, which had been suspended while the severity of the outbreak was greatest, was resumed. Under the alarm of the outbreak, the bazaars had been closed, and the distress arising from cessation of trade was added to the miseries of pestilence. Early in August tradesmen were ordered to re-open their shops, under a penalty of 25 rupees for neglect of obedience.

Of the further progress of cholera in Afghanistan there is no information from the 2nd September, when the disease was still present in Cabul, to the beginning of 1869, when, under date January 4th, it was reported, from Meshed, that the malady was very fatal in Herat, destroying there 200 people daily.

The recurring epidemic activity of cholera in contiguous countries in successive years, each recurrence being notably characterised by diffusiveness through the agency of moving bodies of people, would on the first aspect, and having regard to the common facts of diffusion of the disease, hardly be regarded as disconnected phenomena. Inspector General Dr. John Murray, and others who studied the diffusion of cholera in Northern India from Hurdwar in 1867, while the diffusion

was in progress, came to the conclusion that they were witnessing the beginning of another pandemic extension. Dr. Murray constructed an hypothetical route of the probable progress of the disease beyond the Indian frontier, now before me, so certain did he feel of the migration reaching to Europe. On the other hand Dr. Tholozan, the physician to the Shah of Persia, studying at Teheran the recurrence of cholera in Persia in 1868, and wholly unaware, at the time of the great extension of the disease in Northern India and Eastern Afghanistan the previous year, came to the conclusion that the recurrence was a recrudescence of the cholera already existing in Persia. In like manner, Russian physicians, represented by Dr. Pelikan, the Director of the Imperial Medical Department, studying the outbreak of cholera at Kiev in 1869, irrespective of the remarkable recurrence of the disease in Persia the previous year, came to the conclusion that that outbreak was a recrudescence of the still unexhausted epidemic which had begun in 1865, and of which there were some traces in the province of Kiev the preceding year (1868).

Approaching the study of the recurrences in Persia and Russia from the ascertained local facts alone, and on the assumption that the great epidemic of 1852–56 in Europe was of European origin, there is much to be said in support of the opinions of Dr. Tholozan and Dr. Pelikan.

Cholera in its course through Persia from west to east, appeared in Meshed in December 1867. The next year 1868, at the time of pilgrimage, the city was liable to repeated introductions of the disease from the infected provinces of Mazanderan and Astrabad (where cholera had existed widely the previous years, and had again become active in the spring of 1868), and, thronged with pilgrims, it presented conditions highly favourable to an exceptional development of the disease.

At Kiev, in 1869, cholera also re-appeared at a time when the city was crowded with pilgrims from all parts of the Russian Empire. When the disease first showed itself, and for some time afterwards, it was believed to be *cholera nostras*, so little did the local physicians suspect the existence of any remnants of the preceding epidemic in the province or liability to infection from cholera newly migrating from the east. When the epidemic nature of the malady became obvious, the apparent freedom from cholera of the immense tract of country lying between Kiev and the Persian frontier, preceding the outbreak, seemed to preclude any conception of infection from that source; and on the other hand, the existence of the disease in parts of the province of Kiev in 1868, seemed to indicate certainly a source in recrudescence of an unexhausted epidemic.

If the conclusions of Dr. Tholozan and Dr. Pelikan are confirmed respecting the origin of the recurring cholera of 1868 in Persia and 1869 in Russia respectively, the remarkable problem is presented for consideration *of the successive development in successive years of three great original diffusions of cholera in contiguous countries, each diffusion unconnected with the other by the transmission of the disease through the agency of infected persons from one region to the other* (*such transmission obtaining amidst the various localities within the area of each diffusion*).

The problem, so far as I am aware, is unique in the history of cholera, and before it can be approached with hope of successful solution, it is necessary that any doubt which may rest upon the observations out of which it arises should be fully removed. In other words, until it is shown that the conclusions of Dr. Tholozan and Dr. Pelikan are cleared from such sources of fallacy as may beset them, they should not be accepted without much reservation. Obviously the conditions under which the inquiries which led to the conclusions were made here

become a matter of primary importance. I have already observed that Dr. Tholozan, when he formed the opinion that the outbreak at Meshed in 1868 was solely a recrudescence of the epidemic cholera which had invaded Persia from the west in 1866, was unaware of the invasion of Afghanistan by cholera from India the preceding year (1867). The relation of this prevalence of cholera in Afghanistan to the re-awakened activity of the disease in Persia the following year, except chronologically, is absolutely unknown. Equally unknown is the period of appearance of the disease at Herat, and its relations to the outbreak in Cabul on the one hand, and in Meshed on the other. It may be that the disease died out in Eastern Afghanistan during the severe winter of 1868; but it may be also (and this is perhaps more probable, having regard to the activity of the disease in July and August in Cabul and the vicinity) that its onward course was not arrested there, but that it spread into westward Afghanistan. Persia was, in fact, exposed to certain definite chances of a new invasion of cholera along the route from Herat to Meshed late in 1867 and at the beginning of 1868, and the recurrence of cholera in Meshed in the latter year may have been due either to recrudescence of the declining epidemic in Persia, or to the importation of freshly migrating cholera from India or to both these sources, the recrudescence masking the new migration. This overlapping of epidemics of cholera, so to speak, is not an unknown phenomenon in India.

It is no part of my purpose to attempt to answer this question. I have for object simply to show that before the theory of recrudescence can be accepted, as accounting fully for the phenomena of recurrence and increased epidemic diffusiveness of cholera in Persia in 1868, the possibility of a new invasion of the disease from India having occurred must be eliminated. This, unfortunately, regard being given to the difficulties which beset inquiries of the kind in Persia and Afghanistan, is a remote chance, and the doubt I fear must remain, unless some unexpected source of information become available.

A not unlike doubt rests upon Dr. Pelikan's conclusion as to the recrudescence at Kiev in 1869. The chronological relation of the outbreak in this city to the increased activity of cholera in Persia in 1868, as of that increased activity to epidemic prevalence of the disease in Afghanistan and Northern India the preceding year, had early arrested the attention of English observers. Dr. Pelikan's opinion and the opinion of local observers on the source of the outbreak, as first communicated to the Academy of Medicine, Paris, by Dr. Fauvel, appeared to have been formed without such examination into its relationship with preceding cholera in Persia as appeared to be called for, and without reference to the curious chronological sequence of the outbreak (if known to them) to the epidemic activity of the disease in Northern India and Afghanistan in 1867. In September 1871 Mr. C. Macnamara* had directed attention to the increasing facilities of communication between Russia and Persia, through Caucasia, in relation to the outbreak; and in 1872, looking at the subject from an independent point of view, I had ascertained that much of the Persian trade with Russia had, since 1867, been diverted from the Trebizond route previously followed, and been transferred to a shorter and more quickly traversed route through Transcaucasia to Poti and thence to Russia. With a view of eliciting information, I prepared a report on the subject of the chronological relationship of the outbreak at Kiev with cholera in Persia in 1868 and in India in 1867; and in

* *Indian Medical Gazette, September* 1, 1871.

regard to the trade route between Persia and Russia through Transcaucasia I observed :—

"The re-appearance and diffusion of cholera in South Russia in 1869–71, following close upon or accompanying the most considerable prevalence of cholera in North Persia since the diffusion of the disease in both countries in 1865–67, and also upon the development of a comparatively direct and more quickly traversed route of traffic between Persia and South Russia, is certainly a remarkable coincidence, one of those coincidences, indeed, which, if thoroughly examined, may lead to important results. The data in my possession help little towards such an examination. As I have already remarked, the locality of the reappearance, Kiev, and the absence, so far as I am at present aware, of any extension of cholera across the Russo-Persian frontier, in 1868 and 1869, and, I would add, of its appearance in any of the ports of South Russia, prior to the outbreak at Kiev, seem at first sight to present an insuperable difficulty to the assumption that the diffusion of cholera in Northern Europe in 1869–71, might be an extension of the disease from Persia. But I would observe first, that this difficulty may arise largely from the imperfection of the data at my command; and next, in respect to Kiev, that this city was connected by railroad with Odessa in 1869. Railway communication, I may also state, was opened the same year between Taganrog and Kursk. The facility and rapidity of communication effected by steam, both on land and at sea, unquestionably exercise a very important, and not at all times easily understood, influence upon the dissemination of cholera. In 1866, cholera, in an undetected form, was carried from districts of Germany, by way of Hamburgh, across the German Ocean and this country, and across the Irish Sea, four days' sail into the Atlantic in the case of the steamship "England," and six days' sail in the case of the steamship "Virginia," before it showed itself in its well understood character. Facts like these prove that when the disease appears in the interior of a country, at a distance from a region where it is prevailing epidemically, and even separated from that region by an intervening sea, considerable caution must be exercised before coming to the conclusion that the malady was not imported, if the seat of outbreak in the interior is in free communication with the coast, and with the infected region.

"But, adopting Dr. Pelikan's statement that cholera had never been extinct in Russia, from the introduction of the disease in 1865 to the outbreak at Kiev in 1869, the question arises whether there may not still have been, as was probably the case in Persia in 1868, a re-importation or re-importations of the disease from Persia in 1869 or 1870, which determined its renewed diffusiveness in the latter year and in 1871.

"I have not the data, however, which would permit me to discuss this question. My present object is to direct attention to the coincidence of the outbreak in South Russia in 1869, with the wide prevalence of the disease in North Persia, and the establishment of a direct, and more rapidly traversed route of traffic between South Russia and Persia. I suggest that a more probable explanation of the outbreak in South Russia in 1869 or 1870, and of the subsequent large diffusion of the disease in Northern Europe, is to be sought in the movement of cholera, in some way as yet unknown, along this route into Russia, rather than in the assumption, less consistent with our knowledge of the sources of epidemic diffusion of the disease beyond the limits of India, of the recrudescence of the well-nigh extinguished epidemic of 1865." *

* Report on Recent Diffusion of Cholera in Europe. *Parliamentary Paper*, 8th July 1872.

This report was communicated to the Russian Government, and in a memorandum upon it Dr. Pelikan furnished the details of the outbreak at Kiev which have already been quoted (see page 120); and with respect to the suggested connexion between that outbreak and cholera in Persia, he observed :—"The places in Persia and Russia attacked by cholera were "separated from each other by an immense space entirely free from "cholera, so that the idea of any genetic connexion between the epi-"demics which visited those localities falls of itself to the ground." With respect to the Transcaucasian trade route he further observed :— "This new commercial route has until the present time been of such "little importance as to have exercised scarcely any influence on the "movements of trade along the old route."

I am unable to reconcile Dr. Pelikan's statements that the new commercial route at the period referred to had exercised a hardly appreciable influence upon the movements of trade, with the large increase in the value of the imports across the Transcaucasian frontier in 1868 and 1869, the value of the imports at Astrakhan remaining virtually stationary.*

Dr. Pelikan may simply have meant to convey the impression that the "establishment" of this route indicates only the period when the Russian Government first gave particular attention to its development, and that it does not mark the beginning of any greater flow of traffic along it. I had to regard the coincidence of its establishment with the formation of a new epidemic centre of cholera in South Russia and the wide prevalence of the disease in North Persia, in the light of previous active migration of cholera from India into Afghanistan, and from East Persia into North Persia. The coincidence remains, and it is clear that it was not present to the minds of Russian physicians at the time of the reappearance of cholera at Kiev in 1869.†

Concerning this route I said in the Parliamentary Paper previously referred to :—"The establishment of the route by way of Poti and the "ports of South Russia as the principal line of traffic between Persia "and Russia is a matter which seriously affects the sanitary welfare of "Europe, particularly when considered in connexion with the develop-

*Table showing the Total Value of Imports for Home Consumption by the Transcaucasian Frontier, by Astrakhan, and by Baku, during the six years 1865–69.

Frontiers.	Average Annual Value of Imports, 5 years 1859–63.	1865.	1866.	1867.	1868	1869.
	Sil. Roubles.	Sil. Roubles.	Sil. Roubles.	Sil. Roubles.	Sil. Roubles.	Sil. Roubles.
Transcaucasian Frontier.	5,451,457	7,599,388	8,338,212	8,732,093	9,050,722	10,716,147
Astrakhan - -	1,050,387	1,373,606	1,569,034	1,285,701	1,180,000	1,470,000
Baku - - -	(1863) 741,756 (1864) 1,784,352	780,000	812,000	903,000	486,000	764,000

† Of the new Transcaucasian route, Mr. Consul Palgrave states in his Report on the trade of Trebizond in 1873 :—"To this important line of communication with "Central Asia the Russians first paid serious attention in 1867, and have since "shown the greatest diligence in perfecting both the line itself and the means of "transport. The progressively increasing gains of the new route have been the pro-"portionate losses of the old one ; and the completion this autumn of the railway from "the coast to Tiflis has accelerated the process. Should the Russian administration "continue the line to the Persian frontier, as it intends doing, the Persian transit "viâ Trebizond will be reduced to utter insignificance."—("Reports of Her "Majesty's Consuls," Part 3, 1873, p. 1847.)

" ment of railway communication between Central Europe and the " Russian coast of the Black Sea. By the completion of the line of " railway between Odessa and Kiev in 1869, continuous railway com- " munication was established through Russia, between Northern " Germany, and the principal Russian port on the Black Sea; and, by " the recent completion of a railway between Odessa and Jassy, the " former place has been brought into connexion by way of Cernowitz, " with the railway system of North Germany and Western Europe, and " a direct railway route established between the coasts of the North Sea " and of the Black Sea. In proportion as the projected line of railway " between Poti, Tiflis, Elizabethpol, and Baku, is carried out and " brought into operation, the present augmented speed of traffic between " Persia and Russia will be further accelerated and Persia be brought " into closer connexion with Europe. With the completion of the " Transcaucasian Railway it may be anticipated that this will follow " (to use a phrase of the Medical Officer applied to the relation of the " Continent to this country in respect of infectious diseases), namely, " contagions current in Persia will become current in Europe."

The Poti-Tiflis section of the projected Transcaucasian railway was opened for use partly in 1871, and throughout its entire length in the summer of 1872. In 1873 a weekly steam-service was established between Constantinople and Poti by Persian merchants* ; and on the 25th September 1873 the ceremony of turning the first sod of the first railway in Persia was held at Resht in presence of the foreign consuls and merchants.†

But I am chiefly concerned with the fallacy which underlies Dr. Pelikan's assumption that mere distance, the intervening space being free from cholera, is sufficient, irrespective of other considerations, to establish the absence of any genetic connexion between the re-appearance of cholera at Kiev in 1869, and the prevalence of the disease in North Persia.

The experience of this country since 1865 has tended to show that cholera may be carried greater distances in a latent or undetected form than had previously been suspected. The instances I have already quoted of bodies of emigrants travelling from infected districts of the Continent across the German Ocean, and across England, several days sail out into the Atlantic Ocean, before any sign of cholera was manifested among them, are peculiarly instructive with regard to the question now under consideration. Not less instructive is the instance of cholera being carried from Odessa to Altenburg in 1865. Even more instructive is the history I have given, in the present report, of the relationship of the outbreak of cholera at Southampton, in 1866, to, at the time, wholly unsuspected existence of cholera in Alexandria. I cannot be assured that these instances exhaust the possibilities of distant carriage of cholera in an undetected form. I draw no parallel between the conditions of transit in the instances I have mentioned, and the conditions which exist on the different routes from Persia to South Russia. But it is not to be forgotten that (putting aside the question of the new route) the facilities of communication between Persia by way of the Caspian and the Volga, and from the Volga into the valley of the Don, and thence into Southern Russia were even in 1868 considerable. Astrakhan maintained systematic communication with the Persian coast of the Caspian by steam navigation, during the period of open sea (April to October). Communication was maintained both on the Volga and the Don by steamers, and a short line of

* The *Malta Times*, quoted in the *Times* of 15th October 1873.
† Reuter's Telegrams, the *Times*, September 26th, 1873.

railway between Tzáritzin on the former river, and Kalatch on the latter, connected the traffic of the two streams. From Rostov (on the Don), Kiev was accessible by railway. Kiev in fact, in 1868, was no more remote from the most distant part of the Persian coast of the Caspain, Ashurada, than continuous steam-traffic communications, traversed in a period of time less than three weeks, admitted of.

Again, Dr. Pelikan's statement of the "entire freedom" from cholera of the tract of country intervening between Kiev and North Persia must be read in the light of the means which existed of obtaining information on this subject. It may be at once conceded that there was no such presence of the disease in this tract as marked the migrations of cholera through it in 1830 and 1847. It is not easy to conceive that more than this could be implied. At the period in question the means for ascertaining the existence in Caucasia, beyond the great towns and military posts, of any manifestations of disease were of the most imperfect description. There was hardly a pretence of a registration of deaths,* and the paucity of medical men in the province (greater here, perhaps, than in the conterminous districts of Russia) made even a general knowledge of the prevalence of sickness hardly possible. Moreover, the districts on the borders of the Caspian (Daghestan, Shirwan, Tallish) are principally occupied by Shiah Mahommedans, of whose conditions as to sickness as little is known as of their co-religionists in Persia. Indeed, M. Sobestiansky, writing of the diffusion of cholera in these districts in 1872,† is compelled on this account to limit himself almost entirely to its manifestation in the military posts. Again hardly more, if any more, is known of the states of sickness among many tribes occupying the central mountain districts and the valleys of the Terek and the Kuban. The imperfect knowledge of the progress of cholera in the Caucasia is well understood in the province, and the Imperial Medical Society formed there is at present engaged in endeavouring to recover more satisfactory details on the subject. Until this important work is completed, the state of cholera in Caucasia in 1867, 1868, and 1869 must remain an open question; and it will be doubtful, even then, whether an inquiry made some time after the period under present consideration will remove doubts which could only have been properly dissipated by specific inquiry instituted at the time.

The imperfect knowledge in Russia of cholera in Caucasia is most suggestively shown in Dr. Arkhangelsky's work. The blanks here with reference to the province are numerous and important. The Government of Caucasia does not appear to communicate systematically, if at all, to the Medical Department of the Imperial Government such

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* It is only since 1870 that even in the capital towns of the empire a registration of deaths and causes of death would appear to have come into operation. Writing of St. Petersburg, Dr. Hübner observes:—"Les recherches sur l'état sanitaire de St. Petersbourg en mode statistique ne furent entreprises qù'à partir de l'an 1870 immediatement après le dernier inventaire concernant la population de la capitale, fait dans la courant du Decembre 1869. Ainsi, il n'existait point de notices sur les épidémies dont St. Petersbourg etait en proie jusqu'à l'annee 1870,—si même on trouvait quelques renseignments sous ce rapport—etaient ils médiocres, et, en tout cas, n'insperaient aucune foi." *Du choléra à St. Petersbourg dans le conrant des années* 1870 *et* 1871. (A manuscript placed at my service by Dr. Fredk. J. Mouat.)

† *Transactions of the Imperial Medical Society of Caucasia.* M. Sobestiansky, writing of cholera, in 1872, at Nekhoshvy, district of Baku, observes:—"Although "the origin of the cholera has not been investigated, still we may say with certainty, "that it had a connexion with the epidemic which existed in the districts of Djevat "and Lenkoran, the more so as Nekhoshvy is situated on the route along which "pilgrims went in crowds to Persia and back."

information as it may possess regarding the sickness and mortality of the province. I have found it necessary in this report to supplement the information derived from Dr. Arkhangelsky's work relating to Caucasia with information derived from other sources, especially from the Transactions and Proceedings of the Imperial Medical Society of Caucasia. Of the supplemental information thus given, Dr. Kozlowky's account of the prevalence of cholera in the Fort of Hassav Yourt, district of Terek, in the autumn of 1867, may be especially noted (*see* p. 75). That the fact of so grave an outbreak should have, as is to be inferrred, found no place in the official records of the Imperial Government, indicates the insufficiency of those records, apart from special inquiry, for the discussion of the question I have raised. Indeed, if I read Dr. Sobestiansky aright in the article already referred to, there was cholera in Ciscaucasia in 1869.*

In view of these considerations, the remarkable fact that there is no record of transmission of cholera to Russian territory during the long-continued active prevalence of the disease in the provinces of Mazanderan and Astrabad, notwithstanding its wide diffusion in other directions, can hardly be received as proof that no such transmission took place without further investigation.

It is important that Dr. Pelikan's statement of the entire freedom from cholera of the tract of country intervening between Kiev and North Persia prior to the outbreak of the disease at Kiev in 1869, should not have attached to it the same significance as the expression would have if made of a country like England, where the complete registration of deaths, and large capabilities of obtaining knowledge as to prevalence of sickness, would give some show of justification for the interpretation of the term in its full sense. I say but a show of justification, for even here, with all these advantages, the search into the origin of outbreaks of cholera is one not unattended with difficulty. If the clue could so long escape detection in the outbreak of cholera at Southampton in 1866, how much the more readily might it escape at Kiev in 1869, when the question was complicated by the movements of a great pilgrimage? While undetermined possibilities exist of the carriage of cholera without detection over great distances, I maintain that, if cholera should break out in the interior of a country in free communication with another country in which the disease is active at the time, careful inquiry with respect to importation is needed, if an important source of error is to be avoided, notwithstanding that an extensive tract of country, believed to be free from the disease, may intervene between the new scene of outbreak and the affected country. The absence of such inquiry (in my opinion) vitiates the conclusion of Dr. Pelikan respecting the source of the outbreak at Kiev in 1869.

I have no purpose to discuss other than the data upon which the conclusions of Dr. Pelikan and Dr. Tholozan have been founded with relation to the particular outbreaks referred to. The magnitude of these conclusions appears to me to be altogether out of proportion to the precision of the data upon which they rest. I have already referred to the influence exercised upon the conclusions by the opinion formed respecting the origin of the epidemic of 1852–56 in Europe. It must be obvious that the argument I have urged here with reference to imperfect knowledge of movements of cholera in Caucasia, applies with even greater force to the period of that epidemic when a considerable portion of the province had not submitted to Russia. But the argument is of less force as applied

* He, writing of the diffusion of cholera in the Kuban district in 1872, observes that its general course was the same "as in the former years of cholera, 1866 and 1869.

to the origin of that epidemic than to the origin of the later epidemic. It is important, however, to bear in mind that, of the one recurring epidemic as of the other, the conclusions as to the source under consideration are founded upon defective data, and without reference to a probable concurrence of recrudesence and of the migration of newly invading cholera in the production of the phenomenon to be explained.

The same is true also of the conclusion as to the source of the outbreak at Meshed in 1868.

I can hardly exaggerate, however, the importance of these conclusions as questions of tentative epidemiology, especially as they have been handled by Dr. Tholozan, and I would refer to his lucid monographs: *Origine nouvelle du Choléra Asiatique, ou Débût et Développement en Europe d'une Grande Épidémie Cholérique* (Paris, 1871); and *Durée du Choléra Asiatique en Europe et en Amérique, ou Persistance des Causes Productrices des Èpidémies Cholériques hors de l'Inde* (Paris, 1872). As less readily accessible, I add in an appendix a translation from the Russian of Dr. Arkhangelsky's account of the "Great Cholera Epidemic of 1852–55 in Russia" (See *Appendix*, Note A). From its bearing upon the same subject, I have added also a memorandum on the development of cholera in the basin of the Mississippi in 1873.

I have now brought this Report to a conclusion. In it I have endeavoured to trace from point to point that westward diffusion of cholera in the Eastern hemisphere, which, beginning in 1863, continued uninterruptedly to 1873. Wherever it has been possible to follow the diffusion in detail, its history has been that of a dissemination by human intercourse. Wherever the details of the diffusion have failed, I am unaware of any other suggestion which would explain the successive chronological phenomena. I have no concern in this Report with the conditions which here may have caused the dissemination to become fruitful, and there sterile. I have no concern, moreover, with the conditions which make the disease more diffusive at one period than at another. And in regard to the question of epidemic recrudescence of the malady in countries beyond India, I have limited myself to a discussion of the data bearing upon it derived from certain phenomena of the diffusion I have attempted to describe; adding some information relating to the question which it appeared to me, as being, perhaps, not easily accessible, might be usefully included in the Report. I have touched upon the etiology of cholera only so far as it is elucidated by the chronology of the diffusion and the initial condition of the successive appearances of the disease in different countries.

It is unlikely, having regard to the complexity and often imperfection of the information with which I have had to deal, as well as the difficulty of determining the just value of much of it, that I shall wholly have escaped error. But I venture to hope that the efforts I have made to avoid inaccuracy have not been unsuccessful in reference to the essential features of the Report, and that the facts stated are so recorded as to facilitate the correction of such errors as may be found in it, as other sources of information become available.

App. No. 1.

On Cholera, by Mr. J. Netten Radcliffe.

Tables.

Tables and Notes belonging to Mr. Netten Radcliffe's Report.

Table I.

England and Wales.

Deaths registered from Cholera, Diarrhœa, "Fever," and Zymotic Diseases generally (less Cholera), in England and Wales, during the 26 years, 1847–1872.

Year.	Population.	Cholera.	Diarrhœa.	"Fever."	Zymotic Diseases (less Cholera).
1847	17,150,018	788	11,595	30,094	100,548
1848	17,356,882	1,908	11,067	20,037	99,350
1849	17,564,656	53,273	17,831	18,339	87,851
1850	17,773,324	887	11,468	15,374	77,524
1851	17,982,849	1,132	14,728	17,930	89,000
1852	18,193,206	1,381	17,617	18,641	94,852
1853	18,404,368	4,419	14,192	18,554	85,145
1854	18,616,310	20,097	20,052	18,893	97,038
1855	18,829,000	837	12,770	16,470	87,546
1856	19,042,412	762	13,815	16,182	80,613
1857	19,256,516	1,150	21,189	19,016	92,484
1858	19,471,291	673	13,853	17,883	110,298
1859	19,686,701	887	18,331	15,877	105,758
1860	19,902,713	327	9,702	13,012	75,522
1861	20,119,314	837	18,746	15,440	87,149
1862	20,371,013	511	11,112	18,721	91,028
1863	20,625,855	807	14,943	18,017	118,924
1864	20,883,889	934	16,432	20,106	117,891
1865	21,145,151	1,291	23,531	23,034	112,657
1866	21,409,684	14,378	17,170	21,104	101,594
1867	21,677,525	922	19,851	16,862	90,067
1868	21,948,713	1,498	29,821	19,701	115,858
1869	22,223,299	702	19,903	18,389	109,899
1870	22,501,316	1,065	25,311	17,910	119,446
1871	22,782,812	866	24,140	15,790	122,164
1872	23,067,835	801	22,219	14,020	108,505
1873	23,356,414	749	21,795	13,553	88,537

Table II.*

Rumania.—Cholera, 1865.

Names of the Districts and Towns.	Duration of Disease.	Attacks.	Deaths.
	Old Style.		
Bakeu, district - -	18 August to 25 September	57	42
„ town - -	24 „ „ 25 „	44	27
Byrlat, town - -	27 „ „ 26 October	268	129
Tutova, district - -	27 „ „ 26 „	10	8
Bolgrad „ - -	2 „ „ 31 „	262	80
Brăila „ - -	4 „ „ 10 September	978	344
„ town - -	19 July „ 10 „	1,812	783
Bukharest, town - -	5 October „ 31 December	438	149
Buzeo, district - -	8 August „ 31 October	178	85
Botosanï „ - -	23 November „ 31 December	69	26
„ town - -	20 „ „ 31 „	575	169
Cahul, district - -	15 August „ 16 November	40	26
„ town - -	1 September „ 2 October	15	8
Călărasï, town - -	2 „ „ 30 „	85	40

* N.B.—As to dates of Tables relating to Rumania, see footnote, p. 51.

Names of the Districts and Towns.	Duration of Diseases.	Attacks.	Deaths.
	Old Style.		
Chilia, town	10 August to 27 October	123	55
Covurluiŭ, district	2–7 August	4	3
Doljiŭ „	9–23 October	11	6
Dorohoiŭ „	1–31 December	186	80
Focsanĭ, town	33 August to 13 September	21	9
Galatz „	24 July „ 28 October	1,090	621
Giurgevo „	27 August „ 2 September	11	9
Ilfov, district	28 October „ 6 November	54	22
Ismail, town	1 August „ 16 October	381	172
Jalomitz, district	16 „ „ 1 November	425	104
Jassy „	10 November „ 31 December	322	112
„ town	24 September „ 31 „	1,760	612
Muscel, district	12 November „ 16 November	5	5
Ploescĭ, town	22-23 October	7	5
Rimnicŭ-Sărat, district	13 August to 24 October	33	11
Rimnicŭ-Săratŭ, town	13 „ „ 27 „	137	16
Renĭ, town	29 July „ 15 September	600	145
Vàlcov, town	1 September „ 4 October	43	17
Vlasca, district	30 August „ 9 September	13	10
		9,917 [? 10,057]	4,782 [? 3,930]

Table III.

Rumania.—Cholera, 1866.

Names of the Districts and Towns.	Duration of Epidemic.	Total.	
		Attacks.	Deaths.
	Old Style.		
Bakeu, district and town	28 May to 15 September.	8,254	3,388
Bolgrad „ „	5 June „ 23 August.	1,114	332
Botosanĭ, district	1 March „ 31 „	874	364
Brăila „	30 June „ 12 September.	507	196
„ town	23 „ „ 13 August.	281	131
Civil Hospital, Braila, town		75	34
Buzĕo, district	30 „ „ 30 September.	6,156	1,618
Cahul, district and town	26 „ „ 22 „	1,756	1,006
Covurluiŭ, district	26 „ „ 24 August.	2,767	1,068
Galatz, town	23 „ „ 16 „	1,291	489
Dîmbovitza, district and town	15 July „ 15 September.	57	66*
Dorohoiŭ „ „		166	46
Faltchei „ „	11 June „ 30 August.	120	1,915
Jalomitza „ „	9 July „ 30 September.	3,790	819
Jassy, district	4 May „ 18 August.	2,981	1,403
Jassy, town, Hospital orfanilor	1 July „ 30 „	2,891	44
Galata, Hospital in	7 „ „ 24 July.	21	—
Golia, „	1 „ „ 18 „	6	3
„ Cholera Hospital	3 „ „ 30 „	21	10
Ilfov, district	13 August „ 25 September.	294	66
Ismail „	10 June „ 8 August.	483	233
„ town	10 „ „ 21 „	294	185
Némtu, district and town	30 March „ 14 September.	1,354	772
San Spiridion hospital in Tĕrgu-Némtu.	28 June „ 1 „	70	28

* So in original return.

Names of the Districts and Towns.	Duration of Epidemic.	Total. Attacks.	Total. Deaths.
	Old Style.		
Roman, district - -	5 June to 18 July.	2,006	1,362
„ town - - -	20 May „ 8 September.	1,131	463
„ Precista Hospital in town	5 June „ 18 July.	11	1
Prahova, district - -	4 July „ 26 September.	1,400	246
Ploescí, town - - -	2 „ „ 2 „	653	397
Sucéva, district and town -	18 March „ 30 „	1,016	502
Tecuciŭ „ „ -		7,428	3,126
Tutova, district - -	2 July „ 31 August.	2,869	1,764
Byrlat, town - - -	2 „ „ 31 „	777	337
Rîmnicu-Vâlcea, district & town	12 August „ 3 October.	376	135
Vasluiŭ, district and town -	14 June „ 13 September.	3,736	1,444
Giurgevo, town - -	4 „ „ 25 August.	177	43
Arges, district - - -	1 August „ 15 November.	263	151
Doljiŭ (penitenciarul Bucovĕt)	9 „ „ 30 September.	51	34
Rîmnicu-Săratu, district -	24 June „ 2 August.	6,355	4,396
„ town -		856	339
Caracal, town - - -	6 „ „ 10 October.	55	29
Teleorman, district - -	6 „ „ 28 August.	70	35
		64,541 [? 64,853]	26,174 [? 29,020]

Table IV.

Rumania.—Cholera, 1872.

District.	Number of Communes infected.	Duration of Disease.	Cholera. Cases.	Cholera. Deaths.
		Old Style.		
Bakeu - -	2	10 August to 12 August -	5	5
Faltchei - -	1	10 „ „ 12 „ -	4	4
Jassy - -	12	15 July „ 3 September	1,022	481
Roman - -	3	15 August „ 16 „	28	12
Vaslui - -	1	3 Sept. „ 9 „	34	22
		Totals -	1,093	524

Table V.

Rumania.—Cholera, 1873.

District.	Number of Communes infected.	Duration of Disease.	Cholera. Cases.	Cholera. Deaths.
		Old Style.		
Argesŭ - -	1	25 August to 15 September	4	3
Bakeu - -	1	19 July „ 20 July -	7	2
Braila - -	4	14 July „ 10 September	89	26
„ town -	—	24 June „ 7 „ -	656	327
Buseo - -	1	16 August „ 10 „	23	2
Cahul - -	2 & town	22 June „ 31 July -	86	34
Covurluiŭ - -	1	1 July „ 3 „ -	5	5
„ Galatz -	—	13 June „ 27 August -	372	240
Dmbovitza - -	2	20 August „ 21 „ -	11	4

District.	Number of Communes infected.	Duration of Disease.	Cholera. Cases.	Cholera. Deaths.
		Old Style.		
Doljiŭ - -	37	22 May to 20 September	4,922	899
„ Crajova -	—	1 June „ 22 August -	542	239
Faltchei - -	3	13 July „ 29 „ -	61	36
Gorgii - -	11	13 „ „ 14 „ -	367	63
Jalomitza - -	4	6 July „ 16 September	453	129
Ilfov - - -	5	18 „ „ 2 „	143	65
„ Bucharest -	—	13 August „ 15 December -	1,420	746
Ismail - -	2	7 July „ 21 August -	75	50
Mehedinti - -	20	17 May „ 31 „ -	682	278
„ Severin -	—	6 June „ 18 „	355	182
Nemtzu - -	10	6 July „ 16 September	244	61
Oltzu - -	1	13 August „ 2 „ -	40	7
Prahova - -	12	19 July „ 10 „ -	330	117
Rom-Sarat - -	1	9 „ „ 7 August -	24	5
Romanati - -	2	30 „ „ 18 September	95	45
Tecuciŭ - -	1	3 August „ 16 August -	11	7
Teliorman - -	7	8 July „ 16 September	311	104
Tutova - -	2	18 „ „ 31 July -	16	9
Vaslui - -	1	15 August „ 31 August -	6	3
Vlasca - -	7	17 „ „ 4 September	120	54
„ Guirgevo -	—	27 June „ 4 „ -	226	103
		Totals -	11,516 [? 11,696]	3,864 [? 3,845]

Table VI.*

European Russia.—Cholera, 1865.

Governments.	Beginning of the Epidemic.	Number of Persons attacked.	Deaths.	Proportion of Deaths to 1,000 Inhabitants.	End of the Epidemic.
	Old Style.				Old Style.
Bessarabia - -	Oct. 1	148	37	0·03	Dec. 5.
Volhynia - -	Aug. 11	2,058	795	0·5	Up to 1 Jan. 1866 (cont.)
Voronej - - -	Nov. 13	51	15	0·01	Dec. 18.
Don Cossacks - -	Oct. 24	79	46	0·04	Jan. 8 (1866).
Ekaterinoslav-with-Taganrog.	„ 16	1,085	437	0·3	Feb. 15 „
Kiev - - -	Sept. 25	6,427	1,527	0·7	„ 17 „
Kursk - - -	Jan. 22 (1866.)	349	141	0·08	April 29 „
Podolia - - -	July 26	2,036	679	0·04	Jan. 21 „
Kharkov - - -	Nov. 15	331	186	0·1	April 21 „
Kherson (also Odessa and Nikolaiev.)	July 29	753	314	0·2	Jan. 31 „
Total - -	- -	13,315	4,177	—	
Province of Kertch-Yenikale (Taurida).	Aug. 17	82	41	—	Up to 27 Oct.

* N.B.—As to dates of Tables relating to Russia, see foot note, p. 51.

Table VII.

European Russia.—Cholera, 1866.

Governments.	Beginning of the Epidemic.	Number of Persons Attacked.	Deaths.	Proportion of Deaths to 1,000 Inhabitants.	End of the Epidemic.
	Old Style.				Old Style.
Archangel	None.				
Astrakhan	Aug. 3	429	225	0·4	Nov. 8.
Bessarabi	April 4	18,543	6,796	6·5	„ 30.
Vilna	July 8	4,533	962	1·0	„ 24.
Vitebsk	„ 13	3,453	1,255	1·5	„ 8.
Vladimir	Aug. 13	106	55	0·05	Oct. 11.
Vologda	July 5	61	31	0·03	Aug. 13.
Volhynia	Jan. 1	8,708	3,221	2·0	Dec. 31.
Voronej	July 13	7,466	2,855	1·4	Nov. 30.
Viatka	Aug. 17	6	1	0·004	Aug. 27.
Grodno	June 11	11,213	3,161	3·3	Oct. 31.
Don Cossacks	July 14	3,273	1,305	1·3	Nov. —
Ekaterinoslav with Taganrog.	June 1	8,517	2,847	2·2	Nov. 30.
Kasan	July 3	406	181	0·1	Oct. 16.
Kaluga	„ 8	181	77	0·08	Nov. 17.
Kiev	March 15	9,734	3,165	1·5	„ 30.
Kovno	July 21	7,084	1,840	1·6	„ 10.
Kostroma	Aug. 1	12	3	0·003	Aug. 7.
Courland	July 23	1,029	513	0·9	Oct. 15.
Kursk	June —	13,201	4,689	2·5	„ —
Livonia	July 7	318	179	0·2	„ 12.
Minsk	May 6	816	248	0·2	Jan. 31 (1867).
Mohilev	July —	984	363	0·4	Nov. —
Moscow	June 16	2,198	1,011	0·6	„ 15.
Nijnigorod	July 22	1,067	481	0·4	Oct. 16.
Novgorod	June 24	1,377	486	0·4	„ 13.
Olonetz	„ 29	649	335	1·1	Sept. 14.
Orenburg	Sept. 3	261	158	0·2	Nov. 13.
Orel	June —	1,068	809	0·5	„ —
Pensa	Aug. 9	785	307	0·3	Oct. 20.
Perm	„ 14	378	108	0·05	„ 8.
Podolia	May 30	28,220	10,513	5·4	Nov. 30.
Poltava	June 1	15,462	5,370	2·7	Oct. 23.
Pskov	July 13	1,083	465	0·6	Sept. 23.
Riazan	Aug. 10	261	159	0·1	Oct. 26.
Samara	„ 5	1,557	822	0·5	Nov. 27.
St. Petersburg	June 14	18,655	4,235	3·7	„ 30.
Saratov	July 16	5,267	2,252	1·3	Oct. 31.
Simbirsk	„ 24	1,736	718	0·6	„ 31.
Smolensk	Aug. 27	43	22	0·2	Nov. 2.
Taurida (with Kertch-Yenikale).	June 15	2,804	995	1·5	Oct. 27.
Tambov	July 8	1,712	751	0·4	Jan. 19 (1867).
Tver	June 26	1,995	861	0·6	Sept. 27.
Tula	July 19	383	149	0·1	Oct. 20.
Ufa*	Sept. 11	80	46	0·04	„ 31.
Kharkov	June 23	3,484	1,315	0·8	„ 31.
Kherson (with Odessa)	„ 14	13,948	5,066	3·4	„ 30.
Tchernigov	„ 25	3,201	871	0·6	„ 23.
Esthonia	July 3	127	68	0·2	„ 25.
Jaroslav	„ 1	79	41	0·04	Aug. 15.
Total	-	208,858 [? 207,953.]	72,386	—	

* A government, with Ufa as capital town, constituted by the division of the former province of Orenburg.

Table VIII.

European Russia.—Cholera, 1867 and 1868.

Governments.	Beginning of the Epidemic.	Number of Persons Attacked.	Deaths.	Proportion of Deaths to 1,000 Inhabitants.	End of the Epidemic.
	Old Style.				Old Style.
Vilna	June 28	546	221	0·2	Oct. 17.
Vitebsk	May 8	65	5	0·006	May 12.
Volhynia	—	349	174	0·1	—
Grodno	Aug. 14	305	142	0·2	Sept. 23.
Kovno	„ 28	227	106	0·1	Nov. 9.
Kursk	„ 20	141	63	0·03	Sept. 12.
Minsk	June 1	4,076	1,360	1·2	Nov. 6.
Riazan	—	14	6	0·004	—
St. Petersburg (with the town of St. Petersburg).	Jan. 1	275	139	0·1	Dec. 31.
Kharkov	June 5	247	82	0·05	Sept. 3.
Total	-	6,245	2,298	—	
1868.					
Kiev	July 29	83	35	0·01	Aug. 15.

Table IX.

Poland.—Cholera, 1867.

Governments.	Beginning of the Epidemic.	Number of Persons Attacked.	Deaths.	Proportion of Deaths to 1,000 Inhabitants.	End of the Epidemic.
	Old Style.				Old Style.
Warsaw	April 9	10,688	3,671	4·0	Oct. 31.
Baletz	?	2,569	1,222	2·6	Dec. 20.
Lomjin	June 12	144	65	0·1	Sept. 22.
Lublin	April 9	4,283	2,130	3·3	Dec. 12.
Petrokov	Aug. 15	842	323	0·5	„ 15.
Plotzk	June 6	3,156	1,304	3·0	Sept. 30.
Radom	?	4,236	2,060	4·2	Oct. 31.
Siedlec	May 30	1,041	469	0·9	„ 31.
Souvalki	Nov. 16	59	21	0·04	Dec. 10.
Total	-	27,018	11,265	—	

Table X.

European Russia.—Cholera, 1869.

Governments.	Beginning of the Epidemic.	Number of Persons Attacked.	Deaths.	Proportion of Deaths to 1,000 Inhabitants.	End of the Epidemic.
	Old Style.				Old Style.
Kiev	Aug. 8	338	162	0·8	Dec. 3.
Kaluga	—	12	—	0·0	—
Kursk	Nov. 27	4	2	0·001	Jan. 8 (1870).
Minsk	Oct. 23	33	26	0·02	Dec. 26.
Moscow	Dec. 25	261	122	0·07	Apr.27(1870).
Novgorod	—	58	25	0·02	—
Orel	Nov. 3	502	293	0·2	Mar. 5(1870).
Poltava	„ 12	4	3	0·002	Nov. 26.
St. Petersburg	—	35	11	0·009	—
Smolensk	Dec. 2	7	7	0·006	Jan. 2 (1870).
Tula	Nov. 1	22	8	0·007	„ 1 (cont. toNov.1870).
Total	- -	1,276	659	—	

Table XI.

European Russia.—Cholera, 1870.

Governments.	Beginning of the Epidemic.	Number of Persons Attacked.	Deaths.	Proportion of Deaths to 1,000 Inhabitants.	End of the Epidemic.
	Old Style				Old Style.
Astrakhan	Aug. 14	655	349	0·8	Oct. 23.
Vilna	Nov. 1	53	27	0·03	Nov. 30.
Vladimir	Aug. 24	288	117	0·09	Dec. 14.
Varonej	July 24	1,312	428	0·02	„ 15.
Viatka	Aug. 31	19	11	0·005	Oct. 14.
Grodno	Oct. 28	222	91	0·09	Nov. 30.
Don Cossacks	July 27	2,823	1,237	1·1	Oct. 7.
Ekaterinoslav - with - Taganrog.	June 1	4,404	1,324	1·0	Nov. 14.
Kasan	Aug. 19	86	44	0·03	„ 26.
Kaluga	„ 8	67	30	0·03	Sept. 12.
Kovno	Nov. 30	20	7	0·006	Dec. 22.
Kostroma	Aug. ?	6	5	0·004	Aug. 29.
Kursk	July 19	667	289	0·2	Dec. 25.
Moscow	Aug. 25	196	101	0·05	Up to 1 Jan. (cont. in 1871).
Nijnigorod	„ 18	454	248	0·2	Sept. 15.
Novgorod	„ 28	7	3	0·003	Aug. 31.
Olonetz	„ 24	2	2	0·007	Nov. 25.
Orenburg	Sept. 8	197	114	0·1	Dec. 16.
Orel	July 1	3,244	2,050	1·3	Nov. 25.
Pensa	Aug. 22	506	235	0·2	„ 30.
Perm	„ 24	215	23	0·01	Sept. 30.
Samara	„ 25	248	161	0·09	Oct. 31.
St. Petersburg	„ 16	1,785	772	0·6	Up to 1 Jan. (cont. in 1871).
Saratov	July 29	1,738	810	0·5	Oct. 18.
Simbirsk	„ 19	147	58	0·04	Sept. 30.
Taurida (with Kertch-Yenikale).	„ 7	1,062	394	0·6	„ 18.
Tambov	Sept. 13	145	75	0·03	Nov. 30.

Governments.	Beginning of the Epidemic.	Number of Persons Attacked.	Deaths.	Proportion of Deaths to 1,000 Inhabitants.	End of the Epidemic.
	Old Style.				Old Style.
Tula - - -	Cont. of the Ep. since Jan. 1.	490	168	0·1	Nov. 18.
Kharkov - - -	July 28	542	180	0·1	Dec. 29.
Kherson (with Odessa) -	„ 21	49	23	0·02	Oct. 9.
Jaroslav - -	Sept. 7	14	10	0·01	Nov. 30.
Total -	- -	21,663	9,386	—	

Table XII.

Poland.—Cholera, 1870.

Governments.	Beginning of the Epidemic.	Number of Persons Attacked.	Deaths.	Proportion of Deaths to 1,000 Inhabitants.	End of the Epidemic.
	Old Style.				Old Style.
Warsaw - - -	Oct. 2	308	122	0·1	Dec. —
Kalisz - - -	Nov. 2	51	20	0·03	„ 12.
Petrokov - -	„ 14	57	20	0·03	„ 7.
Plotzk - - -	„ 16	39	22	0·05	Jan. 15 (1871).
Rradom - - -	Oct. 11	69	34	0·06	Dec. 7.
Total - -	- -	524	218	—	

Table XIII.

European Russia.—Cholera, 1871.

Governments.	Beginning of the Epidemic.	Number of Persons Attacked.	Deaths.	Proportion of Deaths to 1,000 Inhabitants.	End of the Epidemic.
	Old Style.				Old Style.
Archangel - -	July 10	373	152	0·5	Nov. 10.
Astrakhan - -	„ 2	1,612	844	1·8	Oct. 9.
Bessarabia - -		Exempt.			
Vilna - - -	April 5	13,057	5,040	4·9	Dec. 31.
Vitebsk - - -	June 27	3,964	1,296	1·5	Sept. 15.
Vladimir - - -	„ 13	12,386	4,883	3·8	„ 23.
Vologda - - -	„ 23	3,023	1,076	1·1	„ 14.
Volhynia - -	July 25	2,110	692	0·4	Feb. 29 (1872).
Voronej - - -	June 21	28,605	11,007	5·0	Nov. 30.
Viatka - - -	„ 26	3,496	1,378	0·6	Oct. 31.
Grodno - - -	July 1	2,777	1,119	1·1	„ 31.
Don Cossacks.	„ 17	1,557	610	0·6	„ 30.
Ekaterinoslav - with - Taganrog).	„ 13	1,440	591	0·4	Sept. 19.
Kasan - - -	June 25	4,517	1,853	1·1	Oct. 31.
Kaluga - - -	„ 15	4,463	2,050	2·0	„ 20.
Kiev - - -	July 15	10,967	4,511	2·1	Up to 1 Jan.

Governments.	Beginning of the Epidemic.	Number of Persons Attacked.	Deaths.	Proportion of Deaths to 1,000 Inhabitants.	End of the Epidemic.
	Old Style.				Old Style.
Kovna	July 1	1,307	500	0·4	Nov. 17.
Kostroma	June 22	5,600	2,021	1·7	Sept. 19.
Courland	July 4	485	249	0·4	„ 23.
Kursk	„ 4	5,521	1,918	1·0	Dec. 31.
Livonia	June 23	1,994	941	0·9	Nov. 13.
Minsk	July 10	2,528	926	0·8	„ 14.
Mohilev	„ 4	13,113	4,818	5·0	Jan. 31.
Moscow	From the 1 Jan.	23,290	10,410	5·6	Nov. 15.
Nijnigorod	June 21	2,563	1,162	0·9	Sept. 15.
Novgorod	„ 9	2,776	1,075	1·0	„ 30.
Olonetz	June 14	519	295	1·0	Oct. 20.
Orenburg	July 19	13,451	4,264	4·7	Jan. 10 (1872).
Orel	„ 22	2,055	843	0·5	Sept. 30.
Pensa	„ 2	9,527	2,687	2·3	Oct. 31.
Perm	June 11	13,292	3,343	1·5	„ ?
Podolia	Aug. 25	470	173	0·1	Dec. 25.
Poltavia	July 5	1,769	639	0·3	Jan. 31 (1872).
Pskov	March 13	809	246	0·3	Nov. 9.
Riazan	„ 11	7,085	3,436	2·4	Oct. 10.
Samara	June 27	11,724	5,001	2·9	„ 6.
St. Petersburg	From the 1 Jan.	7,158	3,017	2·3	„ 29.
Saratov	June 25	15,981	6,261	3·6	„ ?
Simbirsk	„ 22	2,264	643	0·5	„ 15.
Smolensk	July 1	11,290	4,296	3·8	„ 25.
Taurida	Aug. 18	17	10	0·01	Aug. 31.
Tambov	April 5	34,033	14,477	6·7	Nov. 13.
Tver	June 27	2,231	1,034	0·7	Sept. 13.
Tula	„ 8	8,817	2,543	2·1	Nov. 15.
Ufa	„ 25	6,805	2,128	1·6	Oct. 17.
Kherson	„ 12	4,915	1,360	0·8	Nov. 14.
Kharkov	Aug. 3	592	266	0·2	Jan. 27 (1872).
Tchernigov	July 29	1,052	423	0·3	Oct. 31.
Esthonia	Oct. 1	231	136	0·4	Jan. 29 (1872).
Jaroslav	June 5	13,100	6,238	6·2	Sept. 25.
Total	-	322,711	124,831	—	

Table XIV.

Poland.—Cholera, 1871.

Governments.	Beginning of the Epidemic.	Number of Persons Attacked.	Deaths.	Proportion of Deaths to 1,000 Inhabitants.	End of the Epidemic.
	Old Style.				Old Style.
Souvalki	March 18	4,214	1,418	2·7	Oct. 24.
Lomjinsk	Aug. 25	621	207	0·4	Nov. 21.
Kaiisz	„ 26	51	22	0·03	Oct. 8.
Petrokov	Sept. 25	73	38	0·06	Nov. 17.
Total	-	4,959	1,685	—	

Table XV.

Western Siberia.—Cholera, 1871.

Governments.	Beginning of the Epidemic.	Number of Persons Attacked.	Deaths.	Proportion of Deaths to 1,000 Inhabitants.	End of the Epidemic.
	Old Style.				Old Style.
Tobolsk	July 31	286	83	0·07	Oct. 15.
Tomsk	Aug. 23	573	216	0·3	Nov. 30.
Akmolinsk	„ 30	271	72	0·3	Oct. 16.
Total	- -	1,130	371	—	

Table XVI.

European Russia.—Cholera, 1872.

Governments.	Beginning of the Epidemic.	Number of Persons Attacked.	Deaths.	Proportion of Deaths to 1,000 Inhabitants.	End of the Epidemic.
	Old Style.				Old Style.
Archangel	None.				
Astrachan	Aug. 4	1,697	1,061	2·3	Nov. 15.
Bessarabia	May 1	13,286	4,773	4·3	„ 30.
Vilna	Aug. 5	84	49	0·05	Dec. 15.
Vitebsk	July 1	32	18	0·02	Sept. 20.
Vladimir	„ 15	66	27	0·02	Aug. 16.
Vologda	None.				
Volhynia	May 18	26,842	11,163	6·4	Dec. 6.
Varonej	„ 26	809	303	0·1	Oct. 15.
Viatka	July 9	795	286	0·1	„ 22.
Grodno	„ 9	5,984	2,379	2·2	Dec. 23.
Of the Don Cossacks	„ 18	1,646	725	0·7	Nov. 30.
Ekaterinoslav-with-Taganrog	May 16	23,389	7,629	5·7	Oct. 14.
Kasan	July 7	1,155	532	0·3	Nov. 22.
Kaluga	June 21	429	137	0·1	Oct. 25.
Kiev	From the 1 Jan.	53,300	19,843	9·0	Dec. 19.
Kovno	July 28	1,905	809	0·7	„ 19.
Kostroma	„ 15	21	11	0·01	Sept. 11.
Courland	None.				
Kursk	May 6	3,377	1,065	0·5	Oct. 20.
Livonia	None.				
Minsk	„ 15	7,781	3,039	2·6	Jan. 20 (1873).
Mohilev	April 15	12,665	4,738	5·0	Oct. 31.
Moscow	June 1	1,570	848	0·4	Dec. 31.
Nijnigorod	„ 28	461	274	0·2	Sept. 30.
Novgorod	„ 21	570	173	0·2	Aug. 31.
Olonetz	July 17	360	143	0·5	Nov. 18.
Orenburg (with the Oural District).	Sept. 18	279	182	0·2	Dec. 17.
Orel	May 26	2,927	974	0·6	Sept. 30.
Pensa	Aug. 6	249	101	0·1	Dec. 14.
Perm	July 3	2,371	544	0·2	Oct. 31.
Podolia	March 20	34,296	12,990	6·6	Nov. 30.
Poltava	May 12	39,677	12,458	5·9	Oct. 15.
Pskov	July 13	34	9	0·01	Sept. 24.
Riazan	June 8	23	13	0·008	July 31.
Samara	Aug. 8	669	371	0·2	Oct. 19.
St. Petersburg	June 11	4,871	2,364	1·8	Nov. 30.
Saratov	July 22	2,476	1,422	0·8	Oct. 11.
Simbirsk	Aug. 10	470	171	0·1	Nov. 30
Smolensk	„ 28	72	24	0·02	Oct. 31.

Governments.	Beginning of the Epidemic.	Number of Persons Attacked.	Deaths.	Proportion of Deaths to 1,000 Inhabitants.	End of the Epidemic.
	Old Style.				Old Style.
Taurida (with Kertch-Yenikale).	May 24	4,523	1,769	2·5	Aug. 31.
Tambov	Aug. 11	6	4	0·002	„ 14.
Tver	July 5	595	268	0·2	Dec. 18.
Tula	June 10	1,513	555	0·5	Sept. 19.
Ufa	Sept. 12	16	5	0·004	„ 16.
Kharkov	May 23	9,686	2,631	1·5	„ 28.
Kherson (with Odessa)	„ 15	17,913	5,960	4·2	Dec. 16.
Tchernigov	„ 8	29,122	10,084	6·0	Nov. 16.
Esthonia	July 21	503	220	0·7	Sept. 17.
Jaroslav	Aug. 23	92	52	0·05	„ 21.
Total	-	310,607	113,196	—	

Table XVII.

Poland.—Cholera, 1872.

Governments.	Beginning of the Epidemic.	Number of Persons Attacked.	Deaths.	Proportion of Deaths to 1,000 Inhabitants.	End of the Epidemic.
	Old Style.				Old Style.
Warsaw	Aug. 24	2,842	1,214	1·2	Up to 31 Jan. 1873 (cont.)
Lomjinsk	„ 22	3,547	1,770	3·4	Ditto (cont.)
Lublin	Sept. 11	1,371	546	0·7	Dec. 31.
Petrokov	Oct. 16	570	238	0·3	Up to 28 Feb. 1873 (cont.)
Plotkz	Sept. 17	2,192	872	1·6	Ditto (cont.)
Rodom	Oct. 18	97	25	0·05	Dec. 17.
Suvalki	Sept. 6	193	81	0·2	„ 20.
Siedlec	Oct. 2	4,937	851	1·5	Up to 31 Jan. 1873 (cont.)
Total	-	12,033 [15,749?]	5,280 [5,597?]	—	

Table XVIII.

Poland.—Cholera, 1873.

Governments.	Beginning of the Epidemic.	Number of Persons Attacked.	Deaths.	Proportion of Deaths to 1,000 Inhabitants.	End of the Epidemic.
	Old Style.				Old Style.
Warsaw	May 18	12,795	5,788	5·8	Dec. 31.
Kalisz	Feb. 23	143	81	1·8	April 24.
	June 23	2,811	1,143		Dec. 15.
Keletz	July 1	12,395	5,979	11·3	Nov. 30.
Lomjinsk	„ 3	1,201	550	1·1	„ 19.
Lublin	„ 7	7,603	3,516	5·0	Dec. 31.
Petrokov	June 29	7,427	3,615	5·2	„ 31.
Plotkz	July 2	3,142	1,098	2·3	„ 8.
Radom	April 1	10,210	4,974	9·2	Nov. 30.
Suvalki	Sept. 6	48	26	0·5	Oct. 22.
Siedlec	June 24	5,716	2,963	5·7	Nov. 24.
Total	-	63,491	29,733	—	

Table XIX.

European Russia.—Cholera, 1873.

Governments.	Beginning of the Epidemic.	Number of Persons Attacked.	Deaths.	Proportion of Deaths to 1,000 Inhabitants.	End of the Epidemic.
	Old Style.				Old Style.
Bessarabia	June 20	53	2	0·002	June 23.
Vitebsk	July 20	200	66	0·07	Oct. 31.
Volhynia	June 12	2,424	1,056	0·6	„ 31.
Grodno	„ 7	4,071	1,809	1·8	Dec. 23.
Kiev	Aug. 1	15	10	0·005	Sep. 4.
Courland	Sept. 1	79	41	0·07	Oct. 31.
Livonia	Aug. 4	349	179	0·2	„ 31.
Minsk	June 25	966	399	0·3	Nov. 30.
Mohilev	Sept. 1	215	99	0·1	Dec. 31.
Novogorod	„ 6	126	70	0·07	Oct. 31.
Olonetz	Aug. 16	31	18	0·06	„ 20.
Orel	„ 1	23	11	0·007	Sept. 25.
St. Petersburg	June 20	1,283	626	0·5	Nov. 20.
Esthonia	Aug. 23	12	9	0·03	Sept. 18.
Total	-	9,847	4,395	—	

Table XX.

Italy.—Cholera, 1865, 1866, 1867.

(Exclusive of the former States of the Church, and, in 1865, of Venetia.)

Provinces.	1865.		1866.		1867.	
	Population of Communes attacked.	Deaths.	Population of Communes attacked.	Deaths.	Population of Communes attacked.	Deaths.
Abruzzo Citeriore	27,046	97	49,630	195	169,999	2,354
Abruzzo Ulteriore I.	33,386	3	39,600	9	51,108	427
Abruzzo Ulteriore II.	4,802	3	23,998	76	131,695	687
Alessandria	58,948	97	137,271	74	340,882	1,534
Ancona	201,390	3,138	88,348	7	142,732	76
Arezzo	—	—	—	—	39,508	4
Ascoli Piceno	44,875	15	—	—	48,029	69
Basilicata	36,814	132	4,762	118	242,309	2,464
Benevento	3,859	51	87,148	257	119,783	542
Bergamo	—	—	48,320	30	320,244	5,421
Bologna	109,395	19	109,395	81	162,451	124
Brescia	—	—	11,240	8	351,184	4,179
Cagliari	—	—	—	—	82,113	565
Calabria Citeriore	—	—	18,929	86	42,752	539
Calabria Ulteriore I.	—	—	—	—	63,914	1,359
Calabria Ulteriore II.		—	—	—	6,750	38
Caltanisetta	—	—	64,802	60	223,178	7,209
Capitanata	147,977	2,336	103,922	70	253,832	3,506
Catania	—	—	117,981	687	407,552	12,053
Como	445	3	8,597	12	239,804	2,682
Cremono	—	—	—	—	246,661	2,929
Cuneo	224,783	237	255,775	1,263	—	—
Ferrara	67,988	21	76,464	49	24,402	6
Firenze	126,637	2	5,059	2	152,121	16
Forli	91,050	53	77,643	4	—	—
Genova	14,198	6	363,950	1,522	395,444	1,573
Girgenti	—	—	45,499	98	262,962	12,516
Grossetto	—	—	—	—	5,460	2
Livorno	—	—	96,471	5	96,471	316

Provinces.	1865.		1866.		1867.	
	Population of Communes attacked.	Deaths.	Population of Communes attacked.	Deaths.	Population of Communes attacked.	Deaths.
Lucca	—	—	17,344	1	177,221	78
Macerata	129,161	263	—	—	107,569	182
Mantova	—	—	—	—	37,981	12
Massa e Carrara	—	—	26,388	3	45,185	117
Messina	—	—	19,133	6	137,189	4,483
Milano	50,350	2	202,953	4	772,711	4,296
Modena	61,433	76	29,938	5	—	—
Molise	46,207	165	58,461	522	142,298	935
Napoli	781,413	3,379	826,274	5,393	783,644	1,959
Novara	34,782	3	46,676	21	266,697	2,325
Padova	—	—	—	—	157,099	226
Palermo	—	—	441,890	5,688	566,553	12,533
Parma	47,428	0	63,544	12	225,368	1,714
Pavia	—	—	35,284	8	332,856	2,314
Pesaro e Urbino	45,039	13	—	—	—	—
Piacenza	39,387	1	46,070	8	205,087	1,978
Pisa	—	—	51,057	1	137,838	53
Porto Maurizio	10,736	4	28,139	13	—	—
Principato Citeriore	97,736	30	258,981	749	240,444	1,137
Principato Ulteriore	—	—	84,536	133	176,800	1,476
Ravenna	57,303	2	—	—	74,856	28
Reggio nell' Emilia	58,351	14	14,092	4	86,270	67
Rovigo	—	—	—	—	54,251	62
Siracusa	—	—	—	—	135,960	2,353
Sondrio	—	—	—	—	30,806	71
Terra di Bari	341,030	1,636	159,655	77	549,829	9,291
Terra di Lavoro	228,901	161	357,953	864	382,651	1,494
Terra d' Otranto	80,591	645	115,742	247	366,402	5,226
Torino	246,648	223	284,449	361	495,062	6,049
Tranani	—	—	98,823	734	180,524	3,160
Treviso	—	—	—	—	48,482	11
Udine	—	—	—	—	3,170	1
Umbria	73,662	57	58,354	4	144,162	231
Venezia	—	—	—	—	211,009	543
Verona	—	—	—	—	133,870	172
Vicenza	—	—	—	—	50,932	8
Total	3,677,947	12,901	5,160,620	19,571	12,184,116	128,075
Divisions.						
Piemonte	565,161	560	724,171	1,719	1,102,641	9,908
Liguria	24,934	10	392,089	1,535	395,444	1,573
Lombardia	50,795	5	306,374	62	2,294,266	21,892
Veneto	—	—	—	—	696,794	1,035
Emilia	532,335	86	417,146	163	778,434	3,917
Umbria	73,662	57	58,354	4	144,162	231
Marche	420,465	3,429	88,348	7	298,330	327
Toscano	126,637	2	196,319	12	653,804	1,086
Abruzzi e Molise	111,441	268	171,689	802	495,100	4,403
Campania	1,166,105	3,635	1,614,992	7,396	1,703,322	6,608
Puglie	569,598	4,617	379,319	394	1,170,063	18,023
Basilicata	36,814	132	4,762	118	242,309	2,464
Calabria	—	—	18,929	86	113,416	1,936
Sicilia	—	—	788,128	7,273	1,913,918	54,107
Sardegna	—	—	—	—	82,113	565
Total	3,677,947 [?3,823 751]	12,901 [?12,887]	5,160,620	19,571	12,184,116	128,075 [?127,775]

Total population of Italy :—
1862 (Without Venetia) - - 21,776,953.
1866 (End of year, with Venetia) - - 24,149,766.

Table XXI.

Sweden.*—Cholera and Cholerine, 1866.

1	2	3	4	5	6
Districts.	Communes.	Attacks.	Deaths.	Attacks per 1,000 Population.	Deaths per cent.
Norrbotten - - -	8	116	48	1·54	41·3
Westerbotten - - -	4	34	19	0·37	55·9
Jemtland - - -	1	?	1	?	—
Wester-Norrland - -	12	590	151	4·55	25·6
Gefleborg - - -	10	693	307	4·77	44·3
Stora Kopparberg - -	3	35	2	0·19	5·7
Wermland - - -	26	1,058	484	4·03	45·7
Örebro - - - -	9	144	37	0·87	25·7
Westmanland - - -	8	119	53	1·07	44·5
Upsala - - - -	10	90	46	0·92	51·1
Stockholm - - -	9	86	46	0·66	53·5
Stockholm (city) - - -	1	2,105	655	15·23	31·1
Södermanland - - -	7	56	29	0·42	51·8
Göteborg and Bohus - -	23	3,811	1,359	16·32	35·7
Elfsborg - - - -	30	1,580	439	5·63	26·7
Skaraborg - - -	5	139	44	0·58	31·6
Östergötland - - -	27	1,564	654	6·12	41·7
Calmar - - - -	6	185	45	0·79	24·3
Jönköping - - -	3	314	53	1·69	16·8
Kronoberg - - -	1	2	2	0·01	100·
Halland - - - -	3	9	4	0·07	44·4
Blekinge - - - -	2	10	1	0·07	10·
Christianstad - - -	2	5	4	0·02	80·
Malmöhus - - -	3	36	10	0·11	27·7
Gottland - - -	3	18	10	0·35	55·5
Total - -	216	12,799	4,503	3·07	35·2

* Bidrag till Sveriges Officiel Statistik. Sundhets-Collegii Underdåniga Berättelse. 1866.

Table XXII.

England and Wales, 1866.

Deaths from Cholera and Diarrhœa in Registration Divisions.

Divisions.	Population, 1861.	Registration Districts.		Date of first Death from Cholera.	1866.	
		Number in which Deaths from Cholera occurred.	Number in which no Deaths from Cholera occurred.		Deaths from Cholera.	Deaths from Diarrhœa.
I. London -	2,803,989	36	—	26 June -	5,596	3,147
II. South-Eastern Counties.	1,847,661	57	38	13 June (Southampton).	865	956
III. South-Midland counties.	1,295,515	35	27	11 July (Chiswick).	111	699
IV. Eastern Counties.	1,142,562	27	29	12 July (West Ham).	501	519
V. South-Western Counties.	1,835,714	43	36	26 July (Totnes).	631	892
VI. West-Midland Counties.	2,436,568	42	37	23 April (Bristol).	139	2,007
VII. North-Midland Counties.	1,288,928	21	23	27 July (Gainsborough).	83	772
VIII. North-Western Counties.	2,935,540	33	2	1 May (Liverpool).	2,991	4,518
IX. Yorkshire -	2,015,541	33	20	4 July (Hull)	358	1,964
X. Northern Counties.	1,151,372	22	12	3 July (Sunderland).	610	1,135
XI. Monmouthshire and Wales.	1,312,834	34	14	-May (Llangafelach, Swansea).	2,493	561
England and Wales.	**20,066,224**	**383**	**238**	**23 April -**	**14,378**	**17,170**

Table XXIII.

England and Wales, 1866.

Deaths from Cholera and Diarrhœa in the several Counties.

Counties.	Population, 1861.	Deaths from Cholera.	Deaths from Diarrhœa.
I. London.			
Middlesex (part of) - - -	2,030,814	4,879	2,418
Surrey (part of - - -	579,748	377	569
Kent (part of) - - -	193,427	340	160
II. South-eastern Counties.			
Surrey (extra Metropolitan) -	273,264	82	133
Kent (extra Metropolitan) - -	545,272	284	290
Sussex - - - -	366,836	79	177
Hampshire - - - -	456,654	417	279
Berkshire - - - -	205,635	3	77

Counties.	Population, 1861.	Deaths from Cholera.	Deaths from Diarrhœa.
III. South-Midland Counties.			
Middlesex (extra Metropolitan)	187,325	51	163
Hertfordshire	177,452	9	83
Buckinghamshire	147,207	10	48
Oxfordshire	171,233	4	64
Northamptonshire	231,079	7	107
Huntingdonshire	59,137	1	34
Bedfordshire	140,479	22	92
Cambridgeshire	181,603	7	108
IV. Eastern Counties.			
Essex	379,705	471	200
Suffolk	335,409	15	156
Norfolk	427,448	15	163
V. South-western Counties.			
Wiltshire	236,027	11	67
Dorsetshire	182,193	6	44
Devonshire	589,278	525	375
Cornwall	364,848	21	146
Somersetshire	463,368	68	260
VI. West-Midland Counties.			
Gloucestershire	443,535	39	234
Herefordshire	106,796	2	22
Shropshire	260,409	17	139
Staffordshire	769,541	30	890
Worcestershire	294,953	36	215
Warwickshire	561,334	15	507
VII. North-Midland Counties.			
Leicestershire	243,648	3	209
Rutlandshire	23,479	—	12
Lincolnshire	404,143	48	151
Nottinghamshire	323,784	12	230
Derbyshire	293,874	20	170
VIII. North-western Counties.			
Cheshire	470,174	391	402
Lancashire	2,465,366	2,600	4,116
IX. Yorkshire.			
West Riding	1,530,007	283	1,615
East Riding (with York)	274,425	54	234
North Riding	211,109	21	115
X. Northern Counties.			
Durham	542,125	353	620
Northumberland	343,025	224	355
Cumberland	205,276	32	146
Westmoreland	60,946	1	14
XI. Monmouthshire and Wales.			
Monmouthshire	196,977	204	96
South Wales	699,722	2,033	352
North Wales	416,135	256	113

Table XXIV.

Scotland, 1866.

Deaths from Cholera and Diarrhœa in the several Counties.

Counties.	Population, 1861.	Deaths from Cholera.	Deaths from Diarrhœa.
I. Northern.			
Shetland	31,670	1	3
Orkney	32,395	1	2
Caithness	42,200	—	2
Sutherland	24,157	—	6
II. North-western.			
Ross and Cromarty	82,427	1	15
Inverness	84,902	—	28
III. North-eastern.			
Nairn	8,347	1	3
Elgin	44,218	—	16
Banff	56,020	1	12
Aberdeen	223,344	142	107
Kincardine	34,854	22	15
IV. East-Midland.			
Forfar	206,750	214	125
Perth	133,198	24	45
Fife	155,021	260	60
Kinross	8,731	—	1
Clackmannan	20,122	3	7
V. West-Midland.			
Stirling	88,138	6	49
Dumbarton	54,179	7	20
Argyle	83,859	14	29
Bute	16,331	2	5
VI. South-western.			
Renfrew	168,746	39	106
Ayr	199,063	36	107
Lanark	640,444	11	449
VII. South-eastern.			
Linlithgow	39,045	15	19
Edinburgh	274,093	333	181
Haddington	37,626	24	21
Berwick	36,488	3	13
Peebles	11,300	1	—
Selkirk	10,410	2	8
VIII. Southern.			
Roxburgh	53,722	3	11
Dumfries	75,904	1	23
Kirkcudbright	42,495	1	7
Wigtown	42,095	2	9
Scotland		1,170	1,504

Table XXV.

Ireland, 1866.

Deaths from Cholera and Diarrhœa in the several Counties.

Counties.	Population, 1861.	Deaths from Cholera.	Deaths from Diarrhœa.
Province of Leinster.			
Carlow	51,802	82	18
Dublin	412,032	1,459	369
Kildare	100,388	106	31
Kilkenny	113,065	3	56
King's	95,821	8	28
Longford	90,889	24	20
Louth	111,955	17	39
Meath	83,497	2	13
Queen's	74,088	8	28
Westmeath	56,264	19	16
Wexford	155,611	118	38
Wicklow	84,617	131	37
Province of Munster.			
Clare	155,575	10	45
Cork	557,325	175	168
Kerry	197,086	8	46
Limerick	220,896	155	93
Tipperary	246,948	14	97
Waterford	151,047	13	48
Province of Ulster.			
Antrim	355,201	48	189
Armagh	229,051	8	74
Cavan	171,167	3	17
Donegal	225,022	3	43
Down	272,811	16	126
Fermanagh	98,275	1	13
Londonderry	194,713	3	41
Monaghan	136,539	10	39
Tyrone	248,142	3	44
Province of Connaught.			
Galway	273,939	10	57
Leitrim	95,311	2	6
Mayo	252,558	28	29
Roscommon	186,763	8	14
Sligo	100,166	6	29
Ireland —		2,501	1,911

TABLE XXVI.—EGYPT, 1865.—ÉTAT GÉNÉRAL des décès CHOLÉRIQUES, en ÉGYPTE, pendant l'Épidémie de 1865.*

Villes et Provinces.	Décès. Classifiés par Sexes. Hommes ou Garçons.	Femmes et Filles.	Total.	Classifiés par Croyances. Musulmans.	Chrétiens.	Israélites.	Total.	Commencement de l'Épidémie.	Fin de l'Épidémie.	Durée de l'Épidémie.	Chiffre approximatif de la Population.	Observations Générales.
Alexandrie -	2,263	1,755	4,018	3,299	678	41	4,018	11 Juin -	19 Aout -	69 jours -	180,796	4,018 décès sur une population de 180,796, donnent 22 1/4 0/00.
Caire -	3,400	2,704	6,104	5,487	548	69	6,104	17 „ -	17 Sept. -	92 „ -	282,348	6,104 décès sur une population de 282,348, donnent 21 3/4 0/00.
Ramhlet -	43	40	83	70	13	—	83					
Agiami -	16	2	18	18	—	—	18					
Aboukir -	13	10	23	23	—	—	23					
Rosette -	1,069	1,099	2,168	2,166	2	—	2,168	19 „ -	28 Juillet	39 „ -	21,130	2,168 décès sur une population de 21,130, donnent 107 3/4 0/00.
Damiette -	1,128	1,246	2,374	2,307	67	—	2,374	26 „ -	14 Août -	49 „ -	57,000	2,374 décès sur une population de 57,000, donnent 41 2/3 0/00.
Port-Saïd -	50	10	60	6	54	—	60	28 „ -	3 Juillet	34 „ -		
El-Arich -	19	16	35	34	1	—	35	5 Juillet	26 Sept. -	83 „ -		
Suez - -	48	9	57	18	39	—	57	26 Juin -	7 Août -	42 „ -		
Prov. de Béhéra	1,204	1,037	2,242	2,240	2	—	2,242	20 „ -	19 Sept. -	91 „ -		
Garbié -	5,805	4,376	10,181	10,064	117	—	10,181	20 „ -	12 „ -	83 „ -		
Menoufié -	1,444	1,204	2,648	2,644	4	—	2,648	29 „ -	12 „ -	74 „ -		
Dakalié -	3,858	3,498	7,356	7,272	84	—	7,356	22 „ -	3 Août -	42 „ -		
Charkié -	1,903	1,688	3,591	3,479	112	—	3,591	21 „ -	16 „ -	56 „ -		
Galioubié -	392	307	699	699	—	—	699	25 „ -	5 Sept. -	72 „ -		
Ghizi - -	810	663	1,473	1,473	—	—	1,473					
Benisouelf -	513	518	1,031	1,031	—	—	1,031	2 Juillet				
Fayoum -	718	588	1,306	1,306	—	—	1,306					
Minié -	946	820	1,509	1,766	257	—	1,766	30 Juin -	2 Sept. -	63 „ -		
Assiout -	2,293	2,094	4,387	4,387	—	—	4,387					
Ghirgé -	2,930	2,845	5,775	5,775	—	—	5,775					
Kéné -	1,581	1,503	3,084	3,084	—	—	3,084	23 Juillet				
Cosseir et Esné	408	305	713	713	—	—	713					
	32,854	28,337	60,935	59,361	1,978	110	61,192					

* Réponses à Douze Questions sur le Choléra de 1865 et Egypte. Par M. Colucci Bey, Président de l'Intendance Générale Sanitaire d'Egypte.—Alexandrie, 1866.

Table XXVII.

Prussia.—Cholera, 1866.

Governments and Provinces.	Civil Population of infected Districts, 3 Dec. 1864.	Cholera.		Duration of Prevalence.	Per 1,000 Inhabitants.		Per centage of Deaths to Attacks.	Annual Rate of Mortality per 1,000 Inhabitants.
		Attacks.	Deaths.		Attacks.	Deaths.		
Government of Königsberg	1,024,591	17,290	9,054	22 June—Dec. (begin. of)	16·8	8·8	52	—
„ Gumbinnen	724,252	3,284	1,900	14 July—21 Dec.	4·5	2·6	58	5·9
„ Danzig	489,658	5,251	3,030	8 July—11 Nov.	10·7	6·2	58	17·8
„ Marienwerder	743,714	10,775	5,177	6 June—27 Nov.	14·5	7·0	48	14·6
Province of Prussia	2,982,215	36,600	19,161	6 June—21 Dec.	12·3	6·4	52	11·7
Government of Posen	965,684	25,239	11,855	15 June—30 Nov.	26·1	12·3	47	26·6
„ Bromberg	540,260	16,784	8,306	30 June—30 Nov.	31·1	15·4	49	36·5
Province of Posen	1,505,944	42,023	20,161	15 June—30 Nov.	27·9	13·4	48	28·9
City of Berlin	609,733	8,186	5,457	14 June—17 Nov.	13·4	8·9	66	20·7
Government of Potsdam	955,320	11,350	5,824	June—3 Dec.	11·9	6·1	51	12·3
„ Frankfurt-on-the-Oder	911,095	12,601	6,668	2 June—22 Nov.	13·8	7·7	53	15·3
Province of Brandenburg	2,476,148	32,137	17,949	2 June—3 Dec.	13·0	7·2	56	14·2
Government of Stettin	665,994	19,503	10,126	29 May—30 Dec.	29·3	15·2	52	25·7
„ Köslin	539,586	3,982	2,328	3 June—5 Dec.	7·4	4·3	58	9·9
„ Stralsund	213,141	3,231	1,648	16 June— Dec.	15·1	7·7	51	12·4
Province of Pomerania	1,418,721	26,716	14,102	29 May—30 Dec.	18·8	9·9	53	16·7
Government of Breslau	1,327,708	23,160	14,391	25 June—31 Dec.	17·4	10·8	62	20·7
„ Oppeln	1,182,381	9,938	3,659	1 July—21 Dec.	8·4	3·1	37	6·5
„ Liegnitz	963,170	4,525	2,707	4 July—21 Dec.	4·7	2·8	60	6·0
Province of Silesia	3,473,259	37,623	20,757	25 June—31 Dec.	10·8	6·0	55	11·0
Government of Magdeburg	735,051	10,715	4,951	9 July—30 Nov.	14·6	6·7	46	16·9
„ Merseburg	847,082	14,364	6,982	2 July—1867	16·9	8·2	49	16·4
„ Erfurt	366,476	2,470	1,462	23 July—14 Nov.	6·7	4·0	59	12·7
Province of Saxony	1,948,609	27,549	13,395	2 July—1867	14·1	6·9	49	13·8
Government of Münster	346,051	168	88	22 July—14 Dec.	0·5	0·3	52	0·7
„ Minden	395,897	1,191	377	11 July—20 Oct.	3·1	0·9	32	3·4
„ Arnsberg	632,749	3,715	1,970	28 June—14 Jan. 1867	5·8	3·1	53	5·6
Province of Westphalia	1,374,697	5,074	2,435	28 June—14 Jan., 1867	3·7	1·8	48	3·5
Government of Cologne	464,503	712	386	16 July—Dec. (end of)	1·5	0·8	54	1·7
„ Düsseldorf	1,207,837	5,522	2,452	10 June—15 Feb. 1867	5·5	2·5	44	3·6
„ Coblenz	451,328	3,790	1,167	3 April—23 Nov.	8·4	2·6	31	4·0
„ Treves	514,634	4,831	1,697	2 Feb.—13 Jan. 1867	9·3	3·3	35	3·5
„ Aachen	395,726	1,805	1,021	26 July—13 Dec.	4·6	2·6	57	6·7
Province of the Rhine	2,834,028	16,660	6,723	2 Feb., 1866—16 Feb. 1867	5·9	2·4	40	2·3
Hohenzollern and Jahde	Free from cholera.							
Totals	18,013,621	224,382	114,683	2 Feb. 1866—16 Feb. 1867	12·5	6·4	51	6·1

Table XXVIII.

Prussia.—Cholera, 1867.

(N.B.—The returns for Königsberg, Gumbinnen, Posen, Berlin, Magdeburg, Minden, and Kiel had not been published at the time of compilation of this Table, and are not included in it.)

Governments and Provinces.	Civil Population of infected Districts, 3 Dec. 1867.	Cholera.		Duration of Prevalence.	Per 1,000 Inhabitants		Per-centage of Deaths to Attacks.	Annual Rate of Mortality per 1,000 Inhabitants.
		Attacks.	Deaths.		Attacks.	Deaths.		
Government of Königsberg -	No return							
„ Gumbinnen -	Ditto.							
„ Danzig - -	463,972	1,098	666	24 June—30 Nov.	2·37	1·44	60·6	3·28
„ Marienwerder -	362,351	453	244	14 June—15 Nov.	1·25	0·67	54·0	1·61
Province of Prussia - -	826,323	1,551	910	14 June—30 Nov.	1·88	1·10	58·7	2·51
Government of Posen - -	No return							
„ Bromberg - -	138,927	124	53	14 July—15 Oct.	0·89	0·38	42·7	1·21
Province of Posen - -	138,927	124	53	14 July—15 Oct.	0·89	0·38	42·7	1·21
City of Berlin - - -	No return							
Government of Potsdam - -	374,772	15	7	9 July—15 Oct.	0·04	0·02	46·7	0·07
„ Frankfurt-on-the-Oder.	—	—	—	—	—	—	—	—
Province of Brandenburg -	374,772	15	7	9 July—15 Oct.	0·04	0·02	46·7	0·07
Government of Stettin - -	37,556	1	1	25 July—25 July	0·03	0·03	100·0	10·95
„ Köslin - -	—	—	—	—	—	—	—	—
„ Stralsund - -	—	—	—	—	—	—	—	—
Province of Pomerania - -	37,556	1	1	25 July—25 July	0·03	0·03	100·0	10·95
Government of Breslau - -	740,826	1,151	729	26 July—8 Nov.	1·37	0·98	63·3	3·37
„ Oppeln - -	843,610	902	381	6 April—28 June	1·07	0·45	42·2	1·95
„ Liegnitz - -	—	—	—	—	—	—	—	—
Province of Silesia - -	1,584,436	2,053	1,110	6 April—8 Nov.	1·30	0·70	54·1	1·18
Government of Magdeburg -	No return							
„ Merseburg - -	396,317	422	103	6 Sept.—16 Nov.	1·06	0·26	24·4	1·32
„ Erfurt - -	—	—	—	—	—	—	—	—
Province of Saxony - -	396,317	422	103	6 Sept.—16 Nov.	1·06	0·26	24·4	1·32
Government of Münster - -	79,874	3	2	28 Sept.—1 Oct.	0·04	0·03	66·7	2·74
„ Minden - -	No return							
„ Arnsberg - -	557,630	327	193	12 Aug.—28 Dec.	0·53	0·35	59·0	0·92
Province of Westphalia -	637,504	330	195	12 Aug.—28 Dec.	0·52	0·31	59·1	0·81
Government of Cologne - -	315,643	1,429	678	2 June—1 Nov.	4·53	2·15	47·4	5·16
„ Dusseldorf - -	917,875	5,087	2,636	1 Jan.—24 Nov.	5·54	2·87	51·8	3·20
„ Coblenz - -	197,320	17	12	21 March—30 April	0·09	0·06	70·6	0·11
„ Treves - -	63,141	11	7	29 March—16 April	0·17	0·11	63·3	2·11
„ Aachen - -	63,384	133	85	15 Sept.—20 Dec.	2·10	1·34	63·9	5·04
Province of the Rhine -	1,557,363	6,677	3,418	1 Jan.—20 Dec.	4·29	2·19	51·2	2·26
Province of Hohenzollern -	—	—	—	—	—	—	—	—
Jahde - - - -	—	—	—	—	—	—	—	—
Government of Kiel - -	No return							
„ Schleswig - -	59,546	4	4	28 Aug.—6 Sept.	0·07	0·07	100·0	2·56
Province of Schleswig-Holstein.	59,546	4	4	28 Aug.—6 Sept.	0·07	0·07	100·0	2·56

Governments and Provinces.	Civil Population of Infected Districts, 3 Dec. 1867.	Cholera. Attacks.	Cholera. Deaths.	Duration of Prevalence.	Per 1,000 Inhabitants. Attacks.	Per 1,000 Inhabitants. Deaths.	Per-centage of Deaths to Attacks.	Annual Rate of Mortality per 1,000 Inhabitants.
Government of Hanover	—	—	—	——	—	—	—	—
„ Hildesheim	59,260	308	217	27 Aug.—21 Oct.	5·20	3·66	70·5	23·86
„ Luneburg	—	—	—	——	—	—	—	—
„ Stade	—	—	—	——	—	—	—	—
„ Osnabruck	—	—	—	——	—	—	—	—
„ Aurich	—	—	—	——	—	—	—	—
Province of Hanover	59,260	308	217	27 Aug.—21 Oct.	5·20	3·66	70·5	23·86
Government of Cassel	24,426	8	4	17 May—25 May	0·33	0·16	50·0	6·49
„ Wiesbaden	125,332	12	9	10 Sept.—8 Dec.	0·10	0·07	75·0	0·28
Province of Hesse-Nassau	149,758	20	13	17 May—8 Dec.	0·13	0·09	65·0	0·16
Province of Lauenburg	—	—	—	——	—	—	—	—
Totals	5,821,762	11,505	6,031	1 Jan.—28 Dec.	1·98	1·04	52·4	1·05

Note A.

Dr. Arkhangelsky's Account of the Great Cholera Epidemic of 1852–55 in Russia.

(Translated from a reprint of a paper published in the Russian "*Archives of Legal and General Hygienics*, No. 4," December 1871.)

Russia, 1852–55, Dr. Arkhangelsky.

In the two succeeding years 1850–51, following the great cholera epidemic of 1846–49, which had passed into Europe from India through Persia, cholera was met with on the Continent of Europe only as a limited local epidemic, especially in 1851, when the number of places smitten with it was very insignificant, and when the virulence of the epidemic was reduced almost, one might say, to a minimum. From 1852 a fresh series of the most violent cholera epidemics began, which overspread the whole of Europe, and in some places were peculiarly severe.

The question whence arose this third great epidemic in Europe, whether from the remains of the past epidemic or in consequence of a fresh advancing movement of cholera from the place of its birth, India, remains up to this day undecided. This question has an exceedingly great practical importance. The self-origin of Asiatic specific cholera in Europe is denied by all the known facts of the spread of cholera epidemic, and is rejected by the experience of modern medical science. The Constantinople International Sanitary Conference acknowledged as a fact that encroaching Asiatic cholera ("*envahissant*") has never spontaneously developed itself, and has never been met with as an endemic—which must not be confounded with more or less obstinate secondary cholera nests—in any of the undermentioned places, namely, Europe, the Caucasian Provinces, Asiatic Turkey, the whole of the north of Africa, and America, but that it was always brought there from abroad. On these grounds the final solution of the question of the origin of the great cholera epidemic of 1852–55 has great interest with regard to the etiology of cholera. The opinions of epidemiologists respecting this question vary. Some, as, for instance, Professors Griesinger and Lebert, admit a close relation between the epidemics of 1846–49 and those of 1852–55, and acknowledge them to have been but two periods of one and the same epidemic, begun in 1846 in Europe; others, as, for instance, Professors Hirsch and Gezer, explain the epidemic of 1852–55 as a fresh spread from India through Persia into Russia. The former base their opinion on this universally admitted fact that Europe in 1850 and 1851 was not free from cholera; the latter, on this, that from 1849 cholera again increased in India, assumed there a progressive movement, and in 1852

existed in Persia, the Transcaucasus, Russia, and Poland, whence it passed into Prussia.

Professor Gezer, in his "History of Epidemic Diseases," says "that the out-"break of cholera from 1852 to 1856 in all those places where it existed was "exceedingly severe. In India, where this epidemic broke out afresh in 1849, "cholera was in 1852 particularly virulent. In February and March it "appeared in Bombay, in August in Oudh, afterwards in Sumatra and Java. "At one and the same time, by the former route through Persia, Bassora, and "Bagdad, along the coasts of the Caspian Sea, Transcaucasus, and Kur-"distan, it advanced towards the west. Afterwards it spread very quickly "through Russia, Poland, and the greater part of the eastern provinces of "Prussia." (See Gezer, *History of Epidemic Diseases*, St. Petersburgh, 1867, Part 2, p. 169.) Professor Hirsch, in his "Manual of Historico-Geographical Pathology," was evidently the first who said that cholera in the beginning of 1852 was already found on the coasts of the Caspian Sea, whence by various routes it entered Russia and Poland, and by the end of the summer of the same year it reached the eastern provinces of Prussia, Silesia, and Pomerania. (See *Historische Geographische Pathologie*. Erlangen, 1860, vol. iv., p. 125.) This opinion was accepted without critical investigation. Professor Lebert, in spite of his acknowledging the two great epidemics of 1846–49 and of 1852–55 as two periods of one and the same epidemic, says as follows:—"The "cholera in 1850 was exceedingly severe in the greater part of Persia, and in "1851–52 peculiarly so on the southern slope of the Caucasus. The new epi-"demic again passed through Russia, Poland, Prussia, and Scandinavia; "afterwards it visited England, France, the entire coast of the Mediterranean "Sea, Italy, Switzerland, Southern Germany, &c." (See Lebert, *Manual of Practical Medicine;* St. Petersburgh, 1861, Part I., pp. 386–87.)

Doctor Tholozan, physician to the Shah of Persia, in his pamphlet, "Origine "nouvelle du choléra Asiatique, ou début et développement en Europe d'une "grande épidemie cholérique, Paris, 1871," refutes the opinion of Professor Hirsch and shows that in 1852 the cholera could not pass from Persia into Poland through Russia, because, in such a case, its progress must have been peculiarly rapid, and the places which would have been smitten on its advance must have been known to epidemiologists. As the most conclusive proof of the fallacy of the opinion of Dr. Hirsch, Dr. Tholozan states that the delegates of the Russian Government at the Constantinople International Sanitary Conference, Dr. E. V. Pelikan, Director of the Medical Department of the Ministry of the Interior, Drs. Lentz and Bykov, admitted the spread of cholera from Persia into Russia only in the three epidemics of 1823, 1830, and 1847; and had the cholera of 1852 reached Russia from Persia they would have acknowledged it at the Conference. Setting aside the opinion of Dr. Hirsch, Dr. Tholozan endeavours to prove that this epidemic arose in the kingdom of Poland, and, consequently, is of European origin; but such a conclusion will not bear investigation. Is it, for instance, possible to talk of the European origin of potatoes, when it is historically known that they were originally introduced from America, and that they do not exist in an uncultivated state in Europe? Should the cultivation of potatoes under certain circumstances be prohibited, they would soon disappear from the continent of Europe, and for their fresh cultivation in Europe it would be necessary to introduce them afresh either from America or from other places where their cultivation had been continued, or it would have been necessary to find out a place in Europe in which, in spite of this general prohibition, they might have been secretly cultivated. This new spread of potatoes throughout the whole of Europe from such a place which had preserved the remnant of their cultivation, would it have given the right to assert that potatoes are of European origin? Evidently not. On the same principle it is impossible to talk of the European origin of Indian cholera. Facts proving that out of the modified remnants of cholera epidemics, new and more or less malignant local epidemics may arise under favourable but not yet decided conditions, are already well known; but the fact that the insignificant remnants of an epidemic should be the radiating centre of epidemics, not yielding in extent and malignity to the pandemics spreading directly from India, is not fully recognized by modern science, and does not enjoy popularity among epidemiologists. Hence the questions which the Constantinople International Sanitary Conference had to discuss were as follows:—"To investigate the original causes of cholera, to learn its character

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" and its progress, and to ascertain the chief points whence it emanates; and, " finally, to propose practical means for restricting its progress and eradicating " it from its original birthplace." It is necessary to remark that the Conference began its sittings at the commencement of 1866, when cholera had already passed into Europe and continued to exist in many places, that is, when the question of its passage had already lost for that time its practical importance. Notwithstanding this, the delegate of the French Government, Dr. Fauvel, at the first meeting of the Conference, held February $\frac{1}{13}$, raised a very important question on the possibility of cholera spreading from Mecca to Egypt, and proposed measures demanding instant application ("mésures d'urgence"). Dr. E. V. Pelikan, with reference to the work which would be necessary in order to examine the practical bearings of this proposal, submitted whether it would not be better to discuss the measures proposed by the French delegates at the general meetings of the Conference without giving them any special urgency as regards the spring of 1866. This opinion Dr. Pelikan supported by the following remarks:—

1. It is known from the history of all cholera epidemics that this disease had never made its appearance (from India into Europe) by one and the same route in two successive years; but that, on the other hand, having once reached us, in spite of occasional lapses, it afterwards, without any fresh importation from Asia, broke out with its original malignity in various parts of Europe; and,

2. That our present knowledge of the transmissibility ("transmissibilité") of cholera is in an unsatisfactory state, especially as there are many circumstances entirely unknown to us on which the spread of cholera depends.

For these reasons Dr. Pelikan was of opinion that no scientific gain would accrue from adopting urgent measures ("mésures d'urgence") against the new spread of cholera from Mecca to us, and that the only reason for adopting these measures would be that of self-preservation. It would be better, continued Dr. Pelikan, to discover measures against the spread of the remnants of the cholera of last year, when the proper time arrived for discussing the question. (Proceedings of the International Sanitary Conference at Constantinople. *Archives of Legal and Medical Hygienics*, 1866, No. 3.)

This opinion of Dr. Pelikan, having a most important practical value with reference to the European countries, did not receive full sympathy from the members of the Conference. Meanwhile, there were six sittings of the Conference on the question raised by the French delegates.

The spread of cholera of 1852–55 shows in a most marked manner the importance of the question raised by Dr. Pelikan at the Constantinople Conference for European States. Its further spread in 1866 affords additional proof. The Constantinople Conference admitted "that one person infected with cholera " may be the cause of the spread of the disease." "That the spread of the " epidemic depends more or less upon the favourable or unfavourable con- " ditions of the locality where it exists, in the same way that the extent of the " fire is not proportionate to the spark which originated it, but depends upon " the combustible nature or inflammability of the object attacked. The " stoppage of an epidemic does not depend upon the disease becoming less " violent, but upon its total eradication, or the place where it existed " becoming unable to propagate it." (*Archives of Legal and Medical Hygienics*, 1867, No. 1.)

We will now proceed to investigate the spread of the great cholera epidemic of 1852–55.

After the great epidemic of 1847–49 the cholera of 1850 appeared considerably weaker. In the course of this year it existed in Europe in the following countries: Germany, Austria, Denmark, Sweden and Norway, as an epidemic; in France, especially in the town of Marseilles, in the form of separate cases of attack; also in Russia it appeared in isolated cases in the government of Podolsk, and from the 12th to the 22nd of October, in the town of Kamenetz and its district. The total number of persons smitten with cholera at Kamenetz and its neighbourhood was 38, out of which 14 died; besides the above, separate cholera cases were discovered in the government of Vilna, in the district of Zaslav. The other parts of Europe were free from cholera. In the winter of 1850–51 cholera ceased everywhere, with the exception of Bohemia, in Austria, where it continued through the winter in a comparatively slight degree, but in the summer it spread violently again,

App. No. 1.

On Cholera, by Mr. J. Netten Radcliffe.

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and from the official reports it appears that the number of persons attacked with cholera in 1851 was 53,122. Out of this number 23,225 died. At Prague it appeared together with measles, scarlet fever, small-pox, and typhus fever. At Troppau, in Austria, and Silesia, it was exceedingly severe. In the town of Brunn, in Moravia, there were only a few separate cases of this disease.

At the time when the epidemic in 1851 was at it highest point in Bohemia, the first cases of the disease appeared in the districts Habelschwert and Glatz, lying close to the Bohemian-Moravian frontier. In the district of Rybnik, in Upper Silesia, also bordering on Moravia, according to the testimony of Brefeld, the first cases of cholera appeared August 9; almost at the same time, August 11, it broke out in the district of Ratobov, and spread further on "without any geographical connection"(?). At Glatz cholera appeared August 28, the total number of cases being 29; at Breslau, at the end of September, 287 cases. In the district of Breslau the cholera reached its highest point at the very time when it had almost disappeared in Bohemia. In November cholera disappeared in Silesia, the total number of cases being 884, out of which 431 died (Gezer, *History of Epidemic Diseases*, part ii., pp. 166–168).

In Russia, in 1851, cholera existed in the kingdom of Poland, in the government of Warsaw only. It broke out for the first time in the district of Sieradz September $\frac{6}{18}$. In October it appeared in some places of the Konin, Kalisz, and Petrikov districts; in the beginning of November it broke out in the Wielun and Leczyca districts; afterwards it again appeared in the district of Kalisz in November and December.

The districts of Konin, Kalisz, Syeradz, and Wielun are situated along the Prussian frontier; the latter districts join it. According to the opinion of local physicians cholera entered the kingdom of Poland from Silesia. This opinion is strongly confirmed by the geographical position of the districts visited by cholera, and by the time of its appearance in those places; the towns of Prague, of Breslau, of Kalisz, Tursk, and Kolo, are situated in almost a direct line from south-west to north-east.

At the end of December cholera in the kingdom of Poland decreased, one might almost say disappeared, because the number of persons attacked in 10 towns and four villages was only 196, out of which 96 died. It existed among the poorer classes of the population, living in low and swampy districts, subsisting on unwholesome food, especially on potatoes, which were diseased in that year.

Besides the above-named places in Europe, cholera appeared in 1851 in Pomerania, where Stralsund greatly suffered; the other parts of Europe were entirely free from cholera.

It would appear, therefore, that the cholera of 1851 was the direct continuation of the epidemic of 1849–50.

During the first weeks of 1852 one might say that there was no cholera in Europe, but this freedom from cholera was only apparent. The cholera poison was not completely eradicated, and on January $\frac{17}{29}$ it broke out afresh in the town of Varta, in the district of Kalisz, and afterwards on $\frac{\text{January } 22}{\text{February } 3}$ at the town of Turak. In both these towns cholera continued up to the middle of March. The number of sick was only 206 persons, out of which 77 died.

After this cholera disappeared, and it was only in the town of Zlochev, in the district of Syeradz, that it continued to appear from time to time in isolated cases, which very seldom ended fatally.

From May $\frac{12}{24}$ cholera greatly increased at Zlochev, and moreover it appeared in the neighbouring towns of Varta, Syeradz, Zdunska-Vola, Zgyerz, and Kalisz, but without any special threatening aspects. From May $\frac{12}{24}$ to July $\frac{8}{20}$ cholera appeared in four districts of the government of Warsaw, viz., Syeradz, Kalisz, Wielun, and Leczyca, where the number of sick was 322, out of which 166 died, The district of Syeradz suffered most, the number of its sick being 256 and dead 134.

In June cholera became slightly more virulent and spread to two new districts, viz., Piowkov and Rava; at Wielun it made no appearance in June; moreover, from $\frac{\text{June } 23}{\text{July } 11}$ [*sic*] it made its appearance at Warsaw where, from this date up to $\frac{\text{June } 30}{\text{July } 13}$, the number of sick was only 30, dead 9. The number

of sick in the five districts of the government of Warsaw, and in the city of Warsaw, in the course of June, was 1,206, out of which 589 died. In this month cholera spread also in Western Prussia, where the first case of the disease appeared in the town of Ostrov, situated close to the frontier of Poland. It appeared there on $\frac{\text{June } 21}{\text{July } 3}$, consequently earlier than in the town of Warsaw, but it appeared in Prussia sooner than it assumed in Poland any severe aspect; because up to $\frac{\text{June } 23}{\text{July } 5}$ the whole number of sick in the government of Warsaw was 615. Out of these 284 died. The districts of Kalisz and Syeradz, situated on the frontier of Prussia, suffered most. In Kalisz the number of sick was 714, dead 369; in Syeradz the number of sick was 330, dead 130.

In the month of July the cholera began to increase in all the districts of the government of Warsaw. The districts of Kalisch and Syeradz suffered most in this month also; at the town of Warsaw cholera reached an alarming height:—

——	Sick.	Dead.
In the district of Kalisz - -	2,689	1,461
„ „ Syeradz - -	2,290	1,018
„ city of Warsaw - - -	5,992	2,143

In the month of July the cholera not only spread into the other governments of the kingdom of Poland, but also entered the governments of Volhynia and Grodno in Russia; these two governments border on the kingdom of Poland. In the governments of Radom, Plotzk, and Lublin, cholera appeared in three districts, but in the government of Augustowo it appeared in one district only; the number of persons attacked with cholera was considerable in the government of Warsaw only.

July.	Sick.	Dead.
In the government of Warsaw -	14,998	6,292
„ „ Radom - -	375	115
„ „ Plotzk - -	132	46
„ „ Lublin - -	37	13
„ „ Augustowo -	3	2
„ „ Volhynia -	5	3
„ „ Grodno - -	18	9

In the month of August, cholera reached in the government of Warsaw its highest point; it also increased in the other governments, and spread among a larger number of districts. In the town of Warsaw it was equally severe in the month of August as it was in the month of July; it is true, however, that the number of sick was smaller, but the number of dead proportionately greater. In the month of August in the town of Warsaw the number of sick was 4,923, dead 2,465.

The following is a tabular view of the epidemic in the kingdom of Poland and in the governments of Russia:—

August.	Sick.	Dead.
In the government of Warsaw -	32,938	15,834
„ „ Plotzk - -	2,798	1,300
„ „ Radom - -	2,184	1,142
„ „ Lublin - -	1,489	501
„ „ Augustowo -	102	51
„ „ Grodno - -	659	203
„ „ Volhynia -	27	10

In the month of September, cholera began to decrease in the government of Warsaw, and increase in the other governments, but it did not reach in any of them to such a degree of virulence as it did in the government of Warsaw. The number of governments visited by it in Russia remained the same.

In the month of October, cholera spread in the following governments of the Russian Empire: Kovno, Minsk, Courland, Livonia, Esthonia, and St. Petersburg; consequently, it occupied the whole of the west of Russia. How destructive cholera was in European Russia, will be seen from the following monthly tables of its ravages:—

In European Russia.	Sick.	Dead.
In July - -	23	12
„ August -	686	213
„ September -	2,224	728
„ October -	1,619	620
„ November -	2,535	951
„ December -	2,571	905
Total -	9,658	3,429

On the whole, the severity of the cholera of 1852 in several parts of Russia varied. It reached, however, its height, not inferior in its fury to the first two epidemics, in the government of Warsaw only, as will be seen from the accompanying Table, where the number of sick and dead is given according to the governments, and the proportion of deaths to population in each:—

	Sick.	Dead.	Deaths per 1,000 Population.
Governments of the kingdom of Poland—			
Warsaw - - - -	72,302	34,992	20·5
Plotzk - - - -	9,095	4,311	8·0
Radom - - - -	9,094	4,242	4·5
Lublin - - - -	11,034	4,143	4·0
Augustowo - - -	2,002	812	1·3
Total - - -	103,527	48,502	10·0
In the Governments of European Russia			
Grodno - - - -	4,283	1,387	1·7
St. Petersburgh - - -	3,685	1,449	1·3
Minsk - - - -	975	342	0·4
Kovno - - - -	581	165	0·2
Livonia - - - -	205	100	0·4
Courland - - - -	128	73	0·1
Volhynia - - - -	356	123	0·09
Vilna - - - -	82	28	0·03
Esthonia - - - -	69	9	0·03
Novgorod - - - -	49	19	0·02
Vologda - - - -	15	6	0·01
Total - - -	10,428	3,701	

(The number of sick and dead in European-Russia in this Table is greater than that shown in the preceding monthly table of the spread of this disease, because the cholera in the months of January and February, 1853, disappeared entirely in some of the governments.)

The spread of the disease in the districts of the government of Warsaw was not alike. It spread mostly in those districts which border on Prussia, or that are nearest to the Prussian frontier, as will be seen from the following Table, showing the number of sick and dead from May $\frac{12}{24}$ to November $\frac{15}{27}$:—

Government of Warsaw.	From the Outbreak of the Disease, May 12 (24) to Nov. 15 (27).		
	Sick.	Dead.	Deaths per 1,000 Population.
Districts:—			
Gostin	7,609	3,974	42·1
Vlotslav	5,619	3,372	28·6
Syeradz	6,791	3,313	27·1
Kalisch	7,436	3,936	26·6
Lovitz	6,337	2,604	24·4
Konin	5,030	2,695	19·6
Wielun	5,269	2,710	19·5
Leczyca	4,937	2,027	13·9
Petrokov	4,588	2,262	13·0
Rava	2,355	1,278	10·5
Warsaw (without the city)	3,518	1,412	9·6
Stanislav	1,534	623	6·8
Warsaw (city)	11,043	4,707	28·7
Total	72,066	34,913	20·4

(After November $\frac{15}{27}$, 1852, the number of sick and dead in the government of Warsaw became very insignificant. There were 236 cases of the former and 79 of the latter.)

It appears from the above Table that the district of Gostin was most violently attacked by cholera, and next to it Vlotslav; both these districts are situated on the left bank of the River Vistula.

The districts of Plotzk, Lipnov, and Pultusk, of the government of Plotzk, situated on the right bank of the River Vistula, were attacked by the cholera at the same time, but in a less degree, namely,—

	Sick.	Dead.	Deaths per 1,000 Population.
Districts:—			
Plotzk	2,113	1,152	11·7
Pultusk	1,763	784	8·1
Lipnov	1,462	681	7·0
Other districts of the government of Plotzk:—			
Mlva	1,668	677	8·0
Prasny	1,019	476	5·7
Ostrolenka	953	484	5·5
Total	8,978	4,254	7·7

After November $\frac{15}{27}$, 1852, the number of sick in the government of Plotzk was 117, dead 67.

The districts of Stanislav, of Warsaw, and of Rava, in the government of Warsaw, forming the eastern part of this government, were least attacked by the cholera as compared with the other districts of the same government. The district of Warsaw, in spite of its containing the greatest epidemic centre—the town of Warsaw, where 28·7 per thousand of the population died—retained in itself, with regard to cholera, the same characteristics as the eastern half of the kingdom of Poland which was attacked by the disease in a more mitigated form than the western, situated on the borders of Prussia. In the government of Radom, up to November $\frac{15}{27}$, cholera reached its highest development in the district of Opochin, where the number of sick was 2,397, out of which 1,247 died = 7·6 per 1,000 of inhabitants; in the district of Lublin, in the government of Lublin, the number of sick was 3,588, out of which 1,352 died = 7·5 per 1,000 of inhabitants; in the district of Augustowo, in the government of Augustowo, the number of sick was only 659, out of which 328 died = 2·6 per 1,000 inhabitants.

The whole of the above statistics show the great practical importance of the study of the influence of local circumstances on the spread of cholera, to which E. V. Pelikan endeavoured to draw the attention of the Constantinople conference by his statement that, to account for the spread of cholera, it is not sufficient to rely upon the present opinion of its transmissibility ("transmissibilité"), because there are many circumstances entirely unknown to us on which the epidemic spread of cholera depends.

We have not sufficient information concerning the gradual spread of the cholera on the other side of the Prusso-Russian frontier, but we have already seen that the time of the appearance of cholera in Prussia coincides with its first appearance in the kingdom of Poland. July $\frac{8}{20}$ cholera appeared in the city of Posen; at Berlin, from the end of July up to the $\frac{6}{18}$th of August there were only four cases of cholera. After that date cholera developed itself there as an epidemic. We are also ignorant of the localities visited by cholera, as well as of the proportion of fatal cases to the population, but there is not the slightest doubt that the cholera of 1852 in Prussia was one of the most severe epidemics. In its fury it was equal to that of 1831. In Prussia, Professor Gezer says that—

	Sick.	Died.	Out of 1,000 Inhabitants.	
			Sick.	Died.
In 1831 -	53,844	30,923	7·70	4·42
In 1852 -	68,431	40,340	7·50	4·42

"In some localities (?), especially in villages," Professor Gezer says, "this time the disease reached fearful magnitude. There were cases in which more than one third of a village was attacked by cholera, and the rate of mortality reached sometimes 80 and even 90 per cent.!"—(Gezer, *History of Epidemic Diseases*, Part II., p. 170.)

Judging by analogy, it would be necessary to conclude that cholera reached its highest point in localities bordering on the kingdom of Poland, and at the same time situated on the left bank of the River Vistula; this may be confirmed by Dr. Gezer's statement that cholera entered Eastern and Western Prussia along the River Vistula. Thus the idea of the new spread of cholera in the kingdom of Poland will not bear investigation.

The entire area of European Russia, situated between our western provinces and Trans-Caucasia, bordering on the frontiers of Persia, was entirely free from cholera. The opinion of Professor Hirsch and other epidemiologists who have adopted this idea without critical investigation is untenable. At the same time we must note that the idea which gave rise to this opinion was the existence of cholera in Persia in 1852, and its appearance on the Persian frontier in Trans-Caucasia, *i.e.*, in an exceedingly small part of Russia, where the word Russia was applied to the whole of the empire, but no notice was taken of the enormous extent of its territories. Statisticians frequently fall into similar errors when they look upon an empire as a unit, without paying the slightest regard to its size and the number of its inhabitants. (*See* Map I.)

We will now investigate when and under what circumstances cholera appeared in 1852 in Russia on the Persian frontier. We have no correct information of the original appearance, progress, and spread of cholera in Persia in 1851–52, but there is not the slightest doubt that cholera did exist in Persia in 1852. From the moment that cholera in Persia began to advance towards the frontiers of Russia, the Russian Consul-General at Tabriz began instantly to report to the Russian Government the progress of the epidemic. It appears from the Consul's reports that in the summer of 1852 the epidemic reached the district of Azerbijan, and appeared in the town of Urmia, in which, in the course of the first 19 days, 215 persons died. (Reports of Russian Consul-General at Tabriz, July 1 to 7, 1852.) Afterwards the disease began to spread to the valley of Urmia, especially in the south, and reached Sulduz and Maragi (at least cholera was met with in the village of Satalmish, distance from Maragi 56 versts). At Sulduz about 60 persons died daily from cholera. It appears from the reports of the governor of Urmia to the Persian government that the number of persons who died of cholera in the district of Urmia

amounted to 3,000. (Report of Russian Consul-General, July $\frac{14}{26}$.) Afterwards cholera appeared at Salmaz and Khoi, and raged there rather severely. (Reports, September 11.) In the course of a month it began to abate. (Report, October 11.) In the beginning of October the epidemic reached the town of Tabriz and began to spread on the road to Nakhichevan. (Report, October 17.) In the course of a further week cholera began to increase at Tabriz, so that 100 persons died daily from the disease; at the same time, in villages situated along the road to Nakhichevan, it began to decrease, but it spread to Saraba, and reached Geshterud and Germerud. (Report, October 24.) At the end of October the number of persons dying daily from cholera reached 300; at the same time the epidemic spread in the direction—1st, Karadag, where it reached Agar and the neighbouring villages; and, 2nd, on the road to Teheran, where it reached Udzhan and Takmendash. (Report, November 3.) At the end of the year the cholera entirely disappeared from the town of Tabriz; the number of dead from cholera at that town was 12,300 persons. Towards the end of the year it again made its appearance at Agar, at Karadag, and continued to exist at Ardebil. (Report, January 5, 1853.)

There is not the slightest doubt, judging by the preceding reports, that in 1852 cholera existed close to the Russian frontier. Between October 17, when the Russian Consul-General reported on the progress of cholera on the Nakhichevan road, and October 24, when the Consul reported the decrease of this disease on the same route, there occurred the first case of the cholera attack at the town of Nakhichevan; on October 20, private Lukha Kharitonov, private of No. 5 battalion of the Grusian regiment of the line, was taken into the military hospital, smitten with cholera, where he died on the same day.

On the 25th October another private of the same battalion was attacked by cholera, taken to the hospital, and died five hours after admission. In the evening of the same day there were three privates of the same battalion attacked by cholera and taken to the hospital; out of this number one died on the following day.

Dr. Popov, who started for the town of Nakhichevan, consequent upon the outbreak of cholera, learned in the town of Erivan that in a Tartar village, Saderakakh, in the government of Erivan (three stations from the city of Erivan), cholera broke out. In consequence of this he stopped at the above-named village, and on the 26th of November personally attended to some of the sick and became convinced of the real existence of the disease; moreover, he was informed by Ali Sultan, the governor of the village, that cholera had appeared there 10 days before, that at first two persons were attacked by it, afterwards four, and then that the number of the sick gradually increased, so that by the 26th of November the number of sick was 65. Out of this number 36 died, four recovered, and 25 remained ill.

From the 20th of October to the 27th of November there were at the military hospital at Nakhichevan 16 cholera cases, out of which number seven died.

From the reports of Dr. Andreevsky, chief of the medical staff in the Caucasus, dated December 19, 1852, and January 10, 12, 1853, it appears that cholera broke out in the following localities:—

——	Broke out.	Disappeared.	Sick.	Dead.
District of Erivan:—				
Village of Sadurak -	November 15 -	December	70	43
„ Muganly -	Half November -	December	6	4
Winter quarters of Kustin	November 28 -	December 11	33	15
Khadoni-Tamir:—				
Village of Daval - -	December 5 -	December 13	20	9
City of Erivan - -	December 13 -	- - -	1	1
„ Ordubat - -	November 29 -	- - -	1	1
Shushin:—				
Village of Bekmenli -	Beginning December	- - -	4	4
„ Hadjali - -	Ditto - -	- - -	3	3
„ Gadjali - -	- - -	- - -	2	2
		Total -	140	82

The city of Ordubat, as well as the villages of Bekmenli, Hadjali, and Gadjali, are situated in the valley of the River Arax, close to the Persian frontier. On this account Dr. Andreevski concluded that the disease had always passed over from Persia, and did not spread from one part of the country into another, because those localities are separated one from another by a very great distance. It is possible to disagree with the conclusions arrived at by Dr. Andreevski, but there is not the slightest doubt that cholera had originally reached us from Persia through one or more places. Here we clearly see that the spread of cholera, if even out of Persia, does not present any serious aspect unless there exist temporary and local circumstances not yet determined which greatly assist the spread of the cholera poison. To assert that the spread of cholera from Persia in 1852 into Trans-Caucasia should have even the remotest relation to the development of the disease in the kingdom of Poland is out of the question.

The cholera epidemic of 1853 in the kingdom of Poland and in European Russia is a direct continuation of the disease of 1852. The advance of the disease in European Russia (without the districts of the Cossacks of the Don) will be shown in the following monthly lists of the sick and dead:—

1853.	Sick.	Dead.
January - -	2,528	949
February - -	922	408
March - -	1,903	786
April - -	3,608	1,516
May - -	4,289	1,901
June - -	12,538	5,223
July - -	73,358	30,269
August - -	104,041	40,318
September -	26,391	10,439
October - -	13,919	4,999
November -	4,362	1,766
December -	676	303

The governments of Kovno and St. Petersburgh (especially the city of St. Petersburgh), in which cholera began in the autumn of 1852, and continued to exist through the course of the whole of 1853, may be considered as the chief points where the cholera poison was conserved. The government of Volhynia, where the disease reappeared in January 1853, and the government of Moscow, where the epidemic began (in the city of Moscow), also in January 1853, may likewise be considered as the new central points from which the wide spread of cholera proceeded. The cholera of 1853 visited the whole of the governments of European Russia, and spread even into the governments of Western Siberia, so that, with regard to its extent, it was no less severe than the epidemics of 1831 and 1848; but as regards particular places visited by it in the above-named governments, and as regards its virulence, it may be classed among the number of rather weak epidemics. In few of the governments only it reached a certain degree of severity, which will be seen from the table below, showing the absolute number of sick and dead in each of the governments from the cholera of 1853, and the proportion of dead in every 1,000 of inhabitants:—

1853.	Sick.	Dead.	Deaths per 1,000 Population.
Kingdom of Poland. Governments:—			
Augustowo -	6,225	2,376	3·8
Lublin - -	2,846	1,241	1·2
Radom - -	742	353	0·4
Plotzk - -	155	76	0·1
Warsaw - -	378	209	0·1
Total - -	10,346	4,255	0·9

1853.	Sick.	Dead.	Deaths per 1,000 Population.
In European Russia.			
Governments:—			
Jaroslav - -	20,620	8,587	9·1
Esthonia - -	4,909	2,232	7·7
Volhynia - -	25,979	9,750	6·7
St. Petersburg -	17,273	7,175	6·5
Kostroma - -	10,212	5,480	5·4
Novgorod - -	7,680	3,686	3·9
Nijnigorod -	9,604	4,302	3·8
Kovno - -	9,382	3,217	7·7
Courland - -	4,935	2,003	3·7
Grodno - -	7,256	2,708	3·4
Moscow - -	10,357	4,327	3·2
Livonia - -	6,318	2,360	2·9
Vladimir - -	8,199	3,159	2·7
Tver - -	6,333	3,505	2·6
Archangel - -	1,222	599	2·6
Vitebsk - -	7,757	1,846	2·5
Vilna - -	5,957	1,917	2·4
Bessarabia - -	4,850	2,059	2·4
Kiev - -	10,232	3,608	2·2
Minsk - -	5,888	2,050	2·2
Pskov - -	3,046	1,212	1·8
Tchernigov -	5,033	2,080	1·5
Penza - -	2,765	1,574	1·5
Podolia - -	5,917	2,143	1·4
Samara - -	3,463	1,834	1·4
Astrachan - -	870	445	1·2
Kazan - -	4,611	1,451	1·1
Smolensk - -	3,672	1,186	1·1
Olonetz - -	663	312	1·1
Mohilev - -	2,388	827	1·0
Viatka - -	4,707	1,722	0·9
Orenburg - -	3,201	1,415	0·8
Poltava - -	4,836	1,441	0·8
Vologda - -	1,289	634	0·7
Simbirsk - -	2,318	767	0·7
Perm - -	3,419	983	0·6
Kaluga - -	1,194	522	0·5
Tambov - -	2,090	929	0·5
Ekaterinoslav -	1,214	456	0·5
Kherson - -	1,197	487	0·5
Saratov - -	1,132	660	0·4
Kursk - -	1,599	678	0·4
Tula - -	802	279	0·3
Riazan - -	909	422	0·3
Kharkov - -	1,154	389	0·3
Orel - -	547	281	0·2
Voronetz - -	679	338	0·2
Taurida - -	110	46	0·07
Total - -	249,788	100,083	
Western Siberia.			
Governments:—			
Tobolsk - -	3,971	1,783	2·1
Tomsk - -	754	312	0·7
Total - -	4,725	2,095	

From the above tables it will be seen that the western part of the kingdom of Poland, in which the cholera of 1852 was very severe, was very slightly

attacked by the cholera of 1853; at the same time even less than the eastern part. In European Russia the north-western provinces and the Volga provinces suffered most. Thus we must notice here also the influence of locality (as being in conjunction with known local temporary circumstances) on the development and spread of the cholera epidemic. The map sketch of the spread of cholera in Russia in 1853 shows this most vividly. See Map 2. Though the transmissibility of cholera as an exceedingly important agent, in connection with other auxiliary circumstances, in causing an extensive spreading of the cholera epidemic, made itself apparent in 1853 with singular force, we must admit that transmissibility alone does not explain why the cholera of 1853 spread throughout the whole of European Russia. It must consequently be conceded that the spread of the cholera poison circulates the epidemic only where the local and temporary circumstances are favourable to the further development of this disease.

Thus, for instance, as St. Petersburg, the cholera epidemic began in October, and continued uninterruptedly with more or less severity up to 1856. At that time the intercourse with Moscow by means of the railway was not interrupted, the transmissibility of the cholera poison was probable at any moment, and in all probability it was so transmitted, but it was followed by no evil results. On the 10th of January 1853 a patient was received at a hospital in Moscow who had been seized with cholera at one of the railway stations. His name was Osipov, and he had just arrived from St. Petersburg. In that part of the hospital where this patient was placed the cholera broke out on the 16th of January. Up to the 24th of January four patients who were already in the hospital, and one of the nurses, were attacked with cholera. On January 25 and 26 two nurses and another patient, and on the 28th of January a washer-woman of this hospital. It was also in the month of January that cholera broke out at Moscow. The whole of the country, however, between St. Petersburgh and Moscow remained free from cholera. At the commencement of the month of May cholera began to spread in the districts of the government of Moscow; in some of these districts the first persons who were attacked by cholera were those who had arrived there from the city of Moscow. At the town of Wenev, of the government of Tula, on the 31st of March, the first person who was seized with cholera was a veteran soldier who had just returned there from Moscow; in the district Epifan the first person sick of cholera was also one who had just arrived there from Moscow. In the governments of Novgorod and Tver, situated between St. Petersburgh and Moscow, the first persons attacked by the disease were those who had arrived there from St. Petersburgh.

In the government of Esthonia, on the 24th of May, the first person who was attacked by cholera was Mr. A. Von Stackelburgh, who had arrived there on the preceding day from St. Petersburg. He died on the following day. On the 28th of the same month his brother was seized with the disease.

In the month of May the battalions marching from St. Petersburgh to Warsaw brought cholera into the district of Luga, of the government of St. Petersburgh, and in the month of May (Messrs. Pskov and Ostrov) into the government of Pskov, and in the month of June the disease reached the government of Vitebsk.

In the month of June cholera was brought into the government of Olonetz by the religious pilgrims; the Alexandro-Svirsky monastery, where a large number of pilgrims assemble, served this time, as in previous epidemics, as the centre for the spread of cholera. The boatmen of the city of Ribinsk also brought the cholera. In the government of Archangel cholera appeared originally among the pilgrims who had returned in a vessel called St. Demetrius from the monastery of Solovietz into the city of Archangel; out of 130 pilgrims 10 were seized with cholera during the passage, and of these two died on the road and six after their arrival in the hospital.

The circumstances under which cholera was carried into the government of Jaroslav are not known, but on the 9th of June cholera appeared at the town of Rybinsk among the boatmen. It increased so rapidly that it produced quite a panic. In consequence of this, notwithstanding that contracts were concluded with the boatmen, there occurred considerable desertion among them, and some of the merchants, as, for instance, Mr. Suraslev, who was bound in that year to deliver corn into the St. Petersburg magazines, were

for some time placed in an exceedingly difficult position; and even a question was raised by the government about the measures to be adopted against the desertion of the boatmen consequent on the spread of the disease. In the month of June, in the government of Kostroma, cholera broke out also among the boatmen on the River Volga, and afterwards spread into the neighbouring villages; at the town of Kostroma the first four persons attacked with cholera were landed from steamers. In the government of Kazan the cholera appeared in the month of June, chiefly among the boatmen who had arrived from Rybinsk; according to the testimony of one of the sick out of a party of 300 boatmen returning from Rybinsk, 30 died on the road. In the government of Simbirsk, in the beginning of July, the peasants who had arrived in ships were the first that were attacked by cholera. In the government of Penza a "burlak" (bargeman) who had just returned to his village was the first who was attacked by the disease; his family was attacked next. In the government of Perm cholera broke out on the 17th of July, after the arrival of steamers from Kazan and Nishni Novgorod. In the government of Astrachan this disease appeared at the commencement of the month of July. As the Local Government Board of Health acknowledged that the cholera epidemic had been spread from the capital towns, the following question was raised, to which a confirmatory answer was given:—Would it be necessary to carry out quarantine regulations in order that cholera might not be allowed to spread into the provinces of Caucasus? Cholera was brought by the emigrants from the interior governments of European Russia into the government of Orenburg on the 15th of July, Tobolsk on the 4th of August, and into that of Tomsk on the 16th of August.

In the governments of Courland (in June) and Vilna (in July) the first cases of cholera occurred at the postal station; in the government of Minsk it occurred on the 18th of May on board ships which had arrived from the town of Pinsk, in the government of Volhynia. In the government of Podol cholera appeared on the 6th of June in a marching regiment, and among the bread bakers of the Selingin regiment, who had arrived at the town of Mohilev. In the government of Kiev it appeared on the 6th July at the town of Kiev among the working men who were engaged in laying down a suspension bridge. In the government of Kursk, on the 2nd July, the first person who was attacked with cholera was a peasant who had returned from Kiev from a religious pilgrimage. In the town of Kremenchug, of the government of Pultowa, cholera broke out on the 21st June among workmen who had arrived there in vessels on the river Dnieper.

But we need not quote any more of these facts in order to prove what an important part human intercourse plays in the spread of cholera under certain circumstances, even over countries of the greatest extent. A great number of such instances may be met with in every outbreak of cholera epidemic, and they would have been even more numerous had more attention been paid to the first circumstances of the earliest outbreak of cholera. But, on the other hand, human intercourse as regards the spread of epidemics loses all its importance when in a given place and in given time we do not meet with all the agencies which assist in the spread of the cholera poison. The cholera years of 1854–55 very clearly confirm this deduction. The appearance of cholera in 1853 in the Caucasus may be quoted as a no less convincing proof of the above statement.

In 1853 cholera continued to exist in Persia. From report (July 26) of the Russian consul at Astrabad it appears that cholera in the month of June broke out in the district of Astrabad, in the village of Gyaz (close to Astrabad), on the shores of the Caspian Sea, distant six versts from the bay. It is asserted that it was brought there from Mazanderan. In the month of August cholera greatly increased in that village, and spread to other villages in the direction of the town of Astrabad. (Consul's report, dated August 25.) In the month of September cholera appeared in the town of Astrabad, where a rather large number of people died of it. (Report, September 25.) In the month of November cholera disappeared both in the above-named town as well as its environs. (Report, January 16, 1854.)

In the month of July an inhabitant of Bakeu, Artemus Popov, engaged on the steam navigation service on the River Kur, died of cholera at Geok-Top, in the Caucasus. On the 23rd of July the wife of a quarantine officer died of

cholera at Beliasuver, in the district of Lenkoran, in addition to which four other persons were attacked with the disease. Cases of cholera attacks continued in this district in the course of the months of July, August, and September. At first it was questioned whether it was really cholera, but at the end of September it was unanimously agreed to be the Asiatic epidemic cholera. Up to October the disease existed in the district of Lenkoran only, but in the month of October it broke out in the town of Shemakh. Dyakov, an inhabitant of Lenkoran, who had arrived there, was one of the first smitten with the disease. In the month of November cholera appeared in the district of Shushin. The monthly returns of the spread of cholera from the official reports furnished by the governor of Shemakhin will be found in the following list:—

——	Sick.	Dead.
In June - -	21	5
„ August -	69	37
„ September -	115	47
„ October	518	202
„ November -	80	44
Total -	803	335

From the Reports of the Local Government Board of Health it appears that cholera existed during the above-mentioned months in the following places:—

——	Sick.	Dead.
Town of Lenkoran - -	36	19
District of Lenkoran - -	720	276
District of Shushin - -	14	11
Town of Shushin - -	10	5
District of Shemakhin - -	13	9
Total - -	793	320

(The difference in numbers of sick and dead from cholera in Transcaucasia in the above Reports is very insignificant, and in all probability arose from other diseases being confounded with that of cholera.)

To determine the question whence the cholera was brought into the district of Lenkoran, whether from Persia or from Russia, we have no means of ascertaining. We may assume the one or the other because, in the month of July, cholera existed on the shores of the Caspian Sea, close to Astrabad, and at Astrakhan. Moreover, this question loses a great deal of its importance from the fact that the disease spread only in a small portion of South-Western Transcaucasia. In the northern part of the Caucasus, that is, in the government of Stavropol, in the district of Mikhilof, not far from Stavropol, in the second half of the month of October, there were a few cases of cholera-seizure. (The actual number of persons attacked is not given in the Reports.) The persons who were first smitten with the disease were those who had just returned from the fair at Stavropol, where, in consequence of the fair, there was a great gathering of the people from localities where cholera existed, such, for instance, as from Rostof, on the River Don, from Novocherkask, &c. Thus it will be seen that the greatest part of the Caucasus was free from cholera, while those places that were attacked were isolated.

The appearance of cholera in 1853 in Western Europe must not be considered as directly resulting from the existence of cholera in the winter of 1852-53 in Russia. It must be granted that in Prussia those localities in which cholera existed during the winter served as nests for its place in the beginning of the ensuing summer. Thus, for instance, in the town of Breslau the disease stopped only on the $\frac{11th}{23rd}$ April, 1853. Professor Gezer says that

the $\frac{11\text{th}}{23\text{rd}}$ April was the last day of cholera in Prussia, but scarcely a month had passed when it broke out afresh in many places of Prussia. On the $\frac{31\text{st May}}{12\text{th June}}$ cholera broke out in Denmark and at Copenhagen, and already, by the $\frac{1}{2}\frac{2}{7}$th June it reached its highest pitch. From Copenhagen it spread in all directions, but especially towards the north. The number of persons attacked by cholera in the whole of Denmark was 10,598. Out of these 6,888 died.

In England cholera appeared first in sea-side places. At Newcastle and Gateshead, afterwards in London, where, from the $\frac{25\text{th June}}{7\text{th July}}$ up to the end of October, 1,562 persons died.

In the month of August cholera appeared in Norway, but only in a few localities, especially however, at Christainia, whence it spread further along the sea-coast, and into the interior of the country. The number of persons attacked by the disease in the whole of the country amounted to 3,794; out of this 2,448 died, or 5·5 per cent. per 1,000 of inhabitants. In the month of August cholera broke out in Holland, Belgium, and France. In September it appeared in Switzerland, where the number of persons attacked by it was 17,327, and dead 8,775.

On board 28 ships which sailed in 1853, at the time of cholera, from England, Holland, France, Bremen, and Hamburgh, with 13,762 passengers, and arrived at New York in America, there died from cholera during the passage 1,141 persons, or 83 out of every 1,000. The cholera was raging most furiously on board these ships whilst they were within certain degrees of latitude and longitude, and decreased when the ships approached the coast. (Gezer; *History of Epidemic Diseases.*)

We have seen by this time that the cholera of 1853 chiefly raged in Northern Europe, or perhaps it would be more correct to say, in the north-western part of Europe.

In the winter of 1853–54 remains of cholera were observed in all those places where it existed in 1853. With the arrival of warm whether out of these remains there again broke out in Europe a fearful epidemic, so that the cholera of 1854 we may consider without the slightest hesitation as the direct continuation of that of the preceding year.

The spread of cholera in European Russia, month by month, in 1854 was as follows:—

1854.	Sick.	Dead.
January - -	493	229
February - -	171	84
March - -	241	120
April - -	537	239
May - -	1,067	505
June - -	3,018	1,274
July - -	6;080	2,764
August - -	10,471	6,554
September -	3,126	1,715
October - -	1,264	587
November -	940	376
December -	829	385
Total -	28,239	13,832

At the commencement of 1854 cholera had ceased in Russia, both in the kingdom of Poland as well as in all the governments of European Russia, with the exception of St. Petersburgh, where it continued uninterruptedly, and, from the month of March, slightly increased. In the month of April it appeared in the government of Tver and of Livonia. Ivan Dimentev, a peasant, travelling from St. Petersburg by railway, was the first who was attacked with cholera in the town of Tver and generally in the whole of the government of Tver; he was attacked with the disease whilst travelling. On the 31st of March he was sent to a hospital, where, on the 2nd of April, at 10 o'clock in the morning, he died. At the hospital, in consequence of want of room, this peasant was placed in the general room, by the side of another peasant, Peter

Federov. On the day of the death of the former, *i.e.*, on the 2nd April, the peasant Peter Federov was attacked with cholera also, and in the evening of the same day he died. On the 10th and 11th of the same month, two patients in the same hospital were attacked with cholera. Afterwards five passengers attacked with cholera, and travelling from St. Petersburgh, were brought from the railway to this hospital, and on the 20th of June another person seized with cholera on a steamer which had arrived from Rybinsk,

In the month of June cholera appeared in the governments of Esthonia, Novgorod, Pskov, Jaroslav, Kostroma, Samara, Nijnigorod ; in the month of July, in the governments of Olonetz, Vladimir, Moscow, Kasan, Simbirsk, Saratov, Orenburg, and Astrakhan. Consequently, cholera spread along the whole bed of the River Volga. In the same month it also spread in the Western governments, that is to say, it appeared in the governments of Kurland, Kovno, Vilna, and Vitebsk; in the month of August it appeared in the governments of Grodno, Poltava, and in the kingdom of Poland, in the government of Augustowo, where it passed from the government of Kovno bordering upon it.

On the whole, the cholera of 1854 in Russia belongs to the number of very weak epidemics. In the whole of the kingdom of Poland the number of persons attacked was 3,286, out of which 1,806 died. In European-Russia it appeared in the following governments :—

1854.	Sick.	Dead.	Deaths per 1,000 Population.
Governments:—			
St. Petersburg -	8,305	3,618	3·4
Moscow - -	5,106	2,848	1·9
Esthonia - -	1,198	523	1·8
Astrakhan - -	1,084	620	1·6
Kovno - -	2,350	1,055	1·2
Courland - -	711	343	0·6
Vilna - -	919	433	0·5
Jaroslav - -	989	510	0·5
Samara - -	1,060	625	0·5
Novgorod - -	596	325	0·4
Nijni-Novgorod -	725	430	0·4
Orenburg - -	825	512	0·3
Livonia - -	430	220	0·3
Tver - -	868	409	0·3
Orel - -	528	264	0·2
Taurida - -	346	141	0·2
Saratov - -	345	243	0·2
Vitebsk - -	330	107	0·1
Grodno - -	203	104	0·1
Kostroma - -	213	89	0·09
Pskov - -	64	39	0·06
Smolensk - -	178	53	0·05
Vladimir - -	136	63	0·05
Kazan - -	171	44	0·03
Simbirsk - -	32	20	0·02
Perm - -	141	39	0·02
Kherson - -	83	20	0·02
Kaluga - -	64	20	0·02
Poltava - -	24	13	0·01
Penza - -	11	7	0·01
Vologda - -	11	5	0·006
Olonetz - -	6	1	0·004
Total - -	28,052	13,743	

The geographical relation between the governments smitten with cholera shows, notwithstanding the weakness of the epidemic, a certain regularity, and indicates that the cholera epidemic, in spite of transmissibility, depends upon certain physical laws which limit the bounds of this transmissibility.

In Persia, in 1854, the spread of cholera was very moderate (Gezer). Close to the Russo-Persian frontier there was no cholera at all. From reports of the Russian Consul in Persia, it appears that cholera broke out at Teheran at the end of the month of September, that is, at the time when the bodies of dead were dug out of the ground with the view of being sent to holy shrines. They were the bodies of those persons who died at Teheran from previous cholera; and the cholera ceased as soon as the exhuming of the bodies ceased. Places through which the caravan carrying these bodies passed also suffered from cholera. Dr. Cloquet, physician to the Shah, stated that in this year cholera broke out at Teheran simply through the exhumation of these bodies.

In Western Europe the cholera of 1854 assumed gigantic proportions, and raged chiefly in the south-western part of the European continent. In the north of Europe cholera existed in a small degree. In the whole of Sweden the number of persons attacked by cholera was 3,038 only; out of these 1,212 died. In Northern Germany cholera hardly existed at all. In England the disease was comparatively slight.

In France the cholera reached its highest degree of virulence, which may be seen from the following statements quoted by Dr. Tholozan, in his pamphlet, from a "*Résumé des Rapports sur les Epidémies de Cholera Morbus des années* 1854 et 1865," by Dr. M. Barth: "The epidemic of 1832 attacked "56 departments, and ended in the same year, having destroyed from 110,000 "to 120,000 human sacrifices. The cholera of 1849 attacked 57 departments, "and destroyed by the end of the same year from 100,000 to 110,000 persons. "The epidemic of 1854, on the other hand, began at the end of October, "1853, and apparently in a short time died out, but in the month of March "it broke out again, quickly spread through the 70 departments, and only "ended in the following year, when the number of its victims was above "140,000 human beings."

In 1854, from reports furnished by Professor Gezer, it appears that cholera infected 4,893 "communes," in which 125,725 persons died. It will be seen from the above that the cholera of 1854 in France, belongs to the most furious epidemics.

In Italy, as Gezer says, cholera reached an unheard-of pitch. In the kingdom of Sardinia, in 1854, the number of persons attacked with cholera was 45,000, out of whom 24,000 died. In Sicily cholera committed fearful havoc. In Lombardy the disease did not reach a very high degree; the whole number of sick was only 3,116, of dead 2,128. In Bavaria the number of sick was 14,874, dead 7,370. Besides this, cholera existed in Spain, Switzerland, Austria, Turkey, and Greece.

In the winter of 1854–55 cholera continued in many places, although in a small degree. With the approach of the warm weather the disease renewed itself with its former power, but in this year as well as the preceding it elected new localities for its most furious attacks. This time Austria became the victim. In Austria, says Drasche, the number of persons attacked with cholera was 662,814, out of whom 270,915 died (Gezer). In Austrian Galicia the number of persons attacked was 128,213, out of whom 52,304 died; with regard to the whole population the number of sick was 27·8 per 1,000 inhabitants. Here we must remark that the eastern part of Galicia was attacked by cholera in a higher degree. The number of sick attacked by it was 30·2 per 1,000, whilst that in the western was 23·7 per 1,000 of the inhabitants (Drasche). The total number of dead in Galicia, with regard to the whole population, was 11·34 per 1,000 inhabitants.

In the Kingdom of Poland the epidemic of 1855 produced considerable havoc; the total number of sick being 77,539, and of dead 39,563. In that year cholera mostly raged in the eastern part of Poland, especially in the government of Lublin, which suffered more than any of the other governments, and where almost half of the above-named casualties occurred. The government of Augustowo suffered least of any. In the town of Warsaw the disease did not reach by far such a degree as in 1852; the total number of persons attacked by cholera in that town was 4,053, of whom 1,780 died.

In European Russia cholera appeared in 35 governments, but not everywhere with the same virulence. The intensity of the epidemic, as expressed in the proportion of dead to the whole of the population in different governments, varied considerably. The epidemic reached its greatest intensity in European

Russia in those localities which border on Austrian Galicia, and form with it one and the same plain.

1855.	Sick.	Dead.	Deaths per 1,000 Population.
Governments:—			
Volhynia -	41,161	16,357	10·9
Tchernigov	35,990	15,331	10·9
Minsk -	25,395	9,264	9·4
Orel -	23,674	10,440	7·2
Kiev -	27,113	10,724	5·9
Podolia -	25,527	10,084	5·2
Grodno -	11,925	4,825	5·8
Kursk -	21,012	9,202	5·0
Taurida -	7,796	3,309	5·0
Kharkov -	18,263	6,154	4·8
Ekaterinoslav	13,172	4,382	4·2
Poltava -	17,764	6,421	3·7
Kherson -	11,517	3,970	3·7
Bessarabia -	8,826	3,598	3·6
Mohilev -	7,921	2,633	3·0
Vilna -	7,048	2,410	2·9
St. Petersburg	5,440	2,936	2·8
Esthonia -	724	577	2·0
Kaluga -	4,758	1,711	1·7
Moscow -	4,923	2,259	1·5
Smolensk -	3,476	1,262	1·2
Kovno -	1,359	617	0·6
Tula -	2,306	645	0·6
Novgorod -	929	421	0·5
Vitebsk -	753	271	0·4
Courland -	453	211	0·4
Livonia -	502	231	0·3
Voronetz -	1,392	623	0·3
Nijnigorod	297	175	0·1
Jaroslav -	258	114	0·1
Vladimir -	181	79	0·06
Tver -	125	61	0·04
Olonetz -	20	9	0·0
Kostroma -	17	10	0·01
Riazan -	8	8	0·006
Total -	331,025	131,327	

The spread of cholera in 1855 by months will be seen from the following Table:—

1855.	Sick.	Dead.
January -	949	606
February -	586	356
March -	753	409
April -	943	482
May -	4,262	1,731
June -	49,038	20,930
July -	139,983	52,554
August -	112,529	44,114
September	17,144	7,735
October -	3,052	1,465
November	1,169	590
December	101	75
Total -	330,509	131,047

In the winter of 1854–55 the disease had continued chiefly in the three governments of St. Petersburgh, Novgorod, and Esthonia. In the month of April it appeared in two other governments, viz., Orlov and Kherson; it broke out first in the town of Nikolaiev, in the government of Kherson, among six soldiers sent from Sebastopol. In the month of May cholera appeared in the kingdom of Poland, that is, in the government of Lublin, in the early part of this month, and in the town of Warsaw and the government of Radom, in the middle of May. In the same month cholera appeared in European Russia in twelve new governments. In the government of Vilna it broke out in the first-half of the month of May, in the district of Kovel during the march, from the kingdom of Poland, of the grenadier division, with recruits. Of these soldiers, 408 men attacked with cholera were sent to the town hospital at Kovel, where 115 of their number died; only 13 persons out of the whole population of that town were attacked with cholera, and three died. The same division spread cholera in other towns situated along the line of march. Thus into the military hospital of Lutz, the division sent 70 men attacked by cholera, and into that of Dubno 31, of whom 8 died. 45 men were sent to the hospital at the town of Rovno, out of whom 23 died. In the district of Baltsk, of the government of Podolia, cholera appeared for the first time in the 4th and 5th divisions of the second Infantry corps, which were then on the march. At the town of Pinsk, of the government of Minsk, it broke out among the reserve regiment of Jagers who were also on their march. On the 11th of May Dr. Schultz, chief medical officer of the district of Jaroslav, arrived at the city of Dorpat, in the government of Livonia. On the 13th of the same month he was attacked by cholera, and on the 20th he died. On the day of his death the daughter of a notary, 17 years of age, residing in the same house where Dr. Schultz lived, was attacked by cholera and died the same day. It is necessary to note that, in the months of May and June, cholera did not exist in the government of Jaroslav, and if we did admit that Dr. Schultz was under the influence of the cholera poison before his arrival at Dorpat, we must admit also that it must have been contracted somewhere during his journey through the governments of Novgorod and St. Petersburg.

The whole of the above statistical information referring to the cholera epidemic of 1852–55 shows that this epidemic belongs to the greatest class of epidemics, and fully deserves the name of the "Third." It cost Europe more than 1,000,000 of persons who became its victims. This, then, is the fatal result to which Europe has been subjected from the petty remains of a past cholera epidemic. This great epidemic places it beyond all doubt that, as long as there exists on the continent of Europe, be it even in the least degree, the cholera poison, there exists also danger for the health of all the European countries. From the monthly tables of the spread of cholera it is clearly shown that it consists of a regular series of increasing and decreasing virulence. The maximum of the disease reaches its height in the summer, and the minimum in the winter months. In winter not only is the number of victims of the epidemic insignificant, but also the number of localities in which cholera breaks out is limited. This time of the year seems to be the best for the adoption of measures calculated to destroy the cholera poison with the least inconvenience to society. It is evident that the whole burden of inconvenience and expense should not fall exclusively upon that portion of the community only in the midst of which the cholera continues to exist, but should be equally borne by all whom the danger threatens. If that is granted, we may be confident of success.

With the arrival of the hot season of the year, cholera, if there are other favourable local conditions for its development, assumes such wide dimensions, and reaches such a degree of virulence, that society's battle with it becomes almost doubtful, the means of defence being insufficient. The movement of the central point of the epidemic in 1852–55, as well as the formation of such a central point in 1852 from the remains of the past epidemic in Western Poland and Eastern Prussia, must not be ascribed to the influence of human intercourse or other changes that may have taken place in the social and hygienic conditions of the population.

In 1853 the centre of the epidemic was already in the North, in 1854 in Western, and in 1855 in Southern Europe, so that the centre of the epidemic

had made, we might say, in that period of time a complete circular movement throughout the continent of Europe. The epidemic of 1852–55 shows in a most convincing manner that the transit of cholera infection or poison is only dangerous when in a given locality there exist all the favourable conditions for the further spread of this poison. If such favourable conditions do exist, then the quarantine measures cannot prevent the transit of the cholera poison; but if they do not exist, then the cholera poison cannot acquire fixity, and the epidemic will not spread, in spite of human intercourse; consequently the quarantine measures in this case are useless.

Thus it will appear that the task of modern epidemiology is to discover what local and temporal circumstances assist the spread of the cholera poison; or at least to discover the means of knowing from certain appearances in a given time the capability or incapability of a certain locality for the spread in it of that poison. Professor Pettenkofer showed the periodical changes of the rise and fall of the level of the ground-water and its connection with the cholera epidemic. Professor Buhl and others show the dependence of the spread of enteric fever on the fall of the level of the ground-water; and lastly, Middendorf, whilst making researches on the Siberian plague at the time of his journey through the steppes of Baraba in Siberia, gives the moisture of the soil as one of the causes of the rise and spread of the Siberian plague. (*Transactions of the Academy of Sciences*, vol. xix.) A hot and sultry summer, he says, is necessary for the outbreak of the Siberian plague in a locality subject to the epizooty. Endeavouring to discover the connexion between the plague and the moisture of the soil, he heard from the inhabitants of Baraba that the Siberian plague is to a certain degree periodical, and that its periodical appearance depends upon the periodical rise and fall of the level of the water in the lake of Gana. Similar changes in the level of the water were observed in other inland lakes of the Aral-Caspian valley, viz., in the Lake of Ala-kul, in the Kirghese steppes, and in the Aral and Caspian Seas. The attention of Russian physicians has been for a long time past called to the coincidence of the epizootics of plague with the epidemics of cholera; this may be regarded as a confirmation of Middendorf's deduction. The changes in the level of the ground water exercise an undoubted influence on the moisture of the land, and by this means on vegetation; consequently, all investigations respecting the rise and fall of the level of the ground water will have the same practical importance for the agriculturist as other meteorological observations. Everything shows the value of such investigations, and since they cannot be undertaken by private enterprise alone, it is incumbent upon the Government to take the first necessary steps for the purpose of organising stations where observations of this kind might be carried out.

The results to which our investigations of the great cholera epidemic of 1852–55 have led us may be summarised under the following heads:—

1. The cholera epidemic is caused by the appearance (through transit) and spread of a special agent—the cholera poison. In that sense the epidemic of 1852–55 is a direct continuation of former epidemics.

2. The decrease and final disappearance of the cholera depends upon the removal of the possibility of the spread of the cholera agent, and not upon its self-exhaustion or change of its qualities.

3. There are certain peculiar temporary and local changes in the soil, not yet known, which, appearing in a certain locality, make that place a receptacle for the cholera poison.

4. These changes constitute the *conditio sine quâ non* of the existence of the epidemic. The degree of the spread of the epidemic depends upon the degree of the development of these changes.

5. The high state of temperature constitutes one of the most important auxiliary conditions. When the highest temperature of the year coincides with the highest degree of the changes of the soil, then the epidemic reaches its greatest virulence; on the other hand, during a low state of temperature the epidemic becomes confined, and does not reach a high degree of malignity.

6. Homogeneous changes in the soil of the land take place simultaneously in more or less extensive districts; and thus the transit of the cholera poison from the points of its existence to fresh localities is clearly

accounted for; in the latter it becomes the actual momentum for the spread of cholera.

7. The hygienic conditions of a locality constitute exceedingly important elements in the development and spread of cholera; but these elements, after all, are only secondary; without the existence of the corresponding changes in the soil they could not be the cause of the outbreak and spread of cholera.

8. Remains of the old cholera epidemic deserve the same particular attention as the fresh introduction of the cholera poison.

9. The changes in the rise and fall of the level of the land water exercise a considerable physico-chemical influence on the soil, and consequently, according to all appearances, they either directly or indirectly prepare the soil for the reception and spread of the cholera poison.

10. Minute investigations of the rise and fall of the level of land water promise to elucidate many dark spots in the etiology of the cholera epidemic.

In conclusion, I beg to offer a few remarks on the method adopted by me whilst investigating cholera epidemics. The unit accepted by me for the comparison of the *size of the localities* infected with cholera is the official unit,—a "government;" the unit of *time*, the period of a year; and the unity of *intensity* of the cholera, the proportion of the dead from the disease in a given government to the whole population of that government. Such a method of investigation has its advantages and disadvantages. Its advantages consist in this, that small particulars do not darken the general character of the distribution of the epidemic, and clearly point out the existence of a special agent having influence on the intensity of the epidemic; but such a method is evidently insufficient if we apply it to the investigation of the influence of the locality itself, its physical nature, geological formation, &c. Such a unit of the locality as a government is too large. Moreover, in the investigation of the spread of cholera, a shorter period should be taken for the unit of time, say a month, since the locality infected with cholera as well as the virulence of the disease, change in every month. Thanks to the assistance of Mr. E. V. Pelikan, I hope shortly to be able to publish such minute investigations.

The statistical information quoted by me referring to Russia has been compiled from the official reports of the governors of governments and medical inspectors; that concerning the kingdom of Poland has been compiled partly from official reports and partly from an extract made by the medical inspector, Dr. Becker, from the annual reports of the late chief medical department in the kingdom of Poland.

Note B.

Memorandum by Dr. Tholozan, Physician to the Shah of Persia, on Cholera in North-East Persia in the years 1867-69.

Route de Teheran à Méched; exploration faite par Mirza Moustafa, Elève du Collége Médical de Teheran.—Ce mémoire comprend une partie hygiénique et topographique que je supprime ici; je ne mentionne que les dates d'invasion du choléra, telles que l'observation en question les a relevés et telles qu'elles ont été communiquées par moi en 1870 ou 1869 à MM. les médecins sanitaires de Russie et de Turquie délégués à Teheran.

Dans les années 1867, 1868, 1869, le choléra parut sur la route de Teheran à Méched dans un grand nombre de localités au commencement de l'été ou à la fin. Je mentionnerai ici les principaux points, omettant les petits villages, dans lesquels en général la maladie se développa presque en même temps que dans les centres de population plus considérables situées aux environs.

1. Khatounabad (40 maisons), à 5 lieues à l'est de Teheran. En 1868 le choléra s'y déclare en Juin; il dure deux mois dans le district environnant. Il fut plus grave cette année qu'en 1867.

2. Heivanekief, tonjours en avançant vers l'est (700 à 800 habitants). Le choléra y fut plus fort en 1867 qu'en 1868 et 1869.

3. Khor, district contenant une centaine de villages. La maladie s'y comporta comme dans le district précédent.

4. Dehnémek (25 maisons), toujours en avançant vers l'orient. En 1867 il n'y eut pas de choléra. En 1868, choléra au milieu de l'été (12 décès). En 1869 de nouveau choléra (5 décès).

5. Lasguird. Choléra intense au milieu de l'été 1867. Moindre en 1868, où il débuta au commencement des chaleurs (Juin) et causa 30 décès. A la fin de l'été 1869 quelques décès de nouveau.

6. Sourkeh, à l'est du précédent, eut le choléra en 1867, 1868, 1869, à la fin de l'été.

7. Semnan, 12,000 habitants. En 1867, 1868, et en 1869 le choléra y parut la fin de l'été.

8. Plusieurs villages assez peuplés situés sur la route entre la localité précédente et la suivante furent aussi attaqués dans ces trois années.

9. Damghan (8,000 habitants). Choléra dès le premier mois d'été (Juin) dans ces trois années. Il a une durée de deux à trois mois, et fut moins intense en 1869.

10. Chahroud (10,000 à 12,000 habitants). Pendant chacune des trois années il y eût le choléra. Deux mois de durée. Intensité moindre en 1869.

11. Sedkourk. C'est le premier village du district de Sebzevar. Il y eût là le choléra au commencement de l'été 1868. La maladie n'y avait pas paru en 1867.

12. Bachten, bourg du district de Sebzevar. Choléra en 1867, 1868, 1869, décroissant d'intensité chaque année.

13. Sebzevar (15,000 habitants). On ne mentionne spécialement que le choléra de 1869, qui commença dans l'été, et dura trois mois en causant deux à trois décès seulement par jour. Mais en 1867 et 1868 le choléra a régné durement dans cette ville.

14. Nichapour (20,000 habitants), dans une magnifique plaine qui contient 600 villages. Choléra en 1867, 1868, 1869, chaque année; il ne dura que deux ou trois mois.

A ce document il est nécessaire de joindre les faits suivants relatifs à Méched et à Téhéran, située chacun à chaque extrémité de la route :—

Méched.—Le choléra, venu en Perse à la fin de 1865 et au commencement de 1866, atteignit cette ville dans sa marche de l'ouest à l'est au commencement de Décembre 1867 ; il y dura deux mois en donnant lieu à 40 ou 50 décès par jour. (J'étais moi-même à Méched l'été 1867, et il n'y avait pas de choléra à cette époque.) De Méched la maladie se porta encore à l'est, en se dirigeant vers Hérat, et elle atteignit Khof, localité située sur la frontière orientale de la Perse ; c'était en 1868. La maladie dura trois mois à Khof.

Dans la même année, 1868, il y eût à Méched et dans les villages environnants un choléra (recrudescence, dans ma pensée, de celui de l'année précédente) qui dura en Juin, Juillet, et Août.

C'est cette même année que Hérat fut atteint. J'ai appris ce fait vers la fin de l'année par une communication de Mr. Alison, Ministre d'Angleterre. Je suppose que l'invasion y eût lieu au plus tôt à la fin de l'été.

Téhéran, qui avait été atteint en 1867 par la marée cholérique venue du nord-ouest, fut de nouveau et cruellement éprouvé en 1868. Le choléra y présenta trois recrudescences ; elle y débuta avec l'été (Juin).

A côté de ces faits en voici un autre important, parce qu'il a été bien observé :—

(*a*.) Boudjnourd, sur la route de Téhéran à Méched (c'est-à-dire vers le milieu et au nord de la route ordinaire), ville de 5,000 à 6,000 habitants. Le choléra fut assez intense en 1868 ; il débuta en Avril au plus tard.

Les faits relatifs au Mazenderan sont les suivants :—

Au printemps 1867, et peut-être même dans les mois d'hiver de cette année, la vague cholérique atteignit ce pays avant Téhéran. Les localités élevées et montagneuses furent peut-être plus frappées que le bord de la mer.

Astérabad, situé à l'extrémité est du pays, fut légèrement atteint au commencement d'Août 1867. Puis la maladie disparut pour reparaître avec force dans l'automne 1868 sur les tribus Turcomanes du voisinage de l'Atrek (Yamoutes). Sur un régiment de 900 hommes à Astérabad il y eut huit cas de choléra et deux décès.

Le choléra, qui avait paru en 1867 dans les villes de Sari, Amol, Barfourouch, s'y développa de nouveau en 1868. En Mai 1868 il existait déjà à Amol. Il

se déclara à Sari, situé à l'est, dix jours après Barfourouch, situé à l'ouest. Amol est entre les deux villes précédentes.

Dans le district de Zérénd, situé sur la route de Téhéran à Hamadan, j'ai reconnu par moi-même en 1870 que le choléra avait existé en 1867, 1868, 1869, à l'époque de la moisson.

Le choléra dans l'année 1868 se montra aux environs d'Isfahan, à Kerman, à Yezd, à Hamadan (Hamadan, 20 Novembre ; Isfahan, fin Novembre ; Yezd, 13 Septembre ; Kerman, 20 Octobre.)

La ville de Tauris, fortement atteinte en 1866, ne présenta dans l'automne 1868 que quelques cas de choléra léger ; tous ont guéri.

South Persia, 1865-69, Major St. John.

Note on Cholera in South Persia.—The following note respecting cholera in South Persia has been received from Major St. John, R.E., of the India Office, who was on special service in South Persia at the period referred to in it :—

"In the autumn of 1865 there was cholera in the warm region south-east of Shiraz, namely, Fasa, Darch, and Lar. A few isolated cases occurred in Shiraz, but the cold weather coming on no outbreak took place, There was no more cholera in South Persia till 1869, when it reappeared in the same district, south-east of Shiraz, in May and June. At the end of the latter month it broke out with great violence at Shiraz, but whether brought from the infected districts to the south-east, or by a large camp which simultaneously arrived from Teheran, is difficult to say. At least a tenth of the inhabitants of the district of Shiraz, that is, the city and neighbouring villages, were carried off. Very few able-bodied men of any but the lowest class were attacked. It was especially fatal to children and old women, and to Africans. Indeed, hardly a negress (one of whom is found in every respectable Persian house) is said to have survived."

Note C.

Memorandum on the Prevalence of Choleraic Disease in the Basin of the Mississippi in 1873.

Basin of the Mississippi, 1873.

In 1873 there was a considerable prevalence of fatal choleraic disease in the basin of the Mississippi. The disease first showed itself in New Orleans in February, and afterwards it appeared in numerous localities along the course of the river and its affluents, in some places causing a large mortality. For example, in Memphis, Tennessee, of 522 deaths, of which an account has been recovered, occurring in the six weeks from the 1st June to the 12th July, 212 were assigned to cholera. The history of the disease and of its distribution is exceedingly imperfect. The most important information relating to it yet published, has been collected by the *American Public Health Association* and printed in the Association volume of reports and papers for 1873.* These include several reports on local occurrences of the disease, a "Report "upon the course of Cholera through 200 Towns and Cities in the Missis-"sippi Valley," by Dr. Adoniram B. Judson, of New York ; and "An Account "of the Epidemic of Cholera during the Summer of 1873 in 18 Counties of the "State of Kentucky," by Dr. Ely MacClellan, of the United States Army Medical Staff. Dr. Judson's report, which is illustrated by a carefully prepared map, embodies facts "which have been derived chiefly from daily and weekly "newspapers of the towns in which cholera made its appearance, and from "manuscript reports of trustworthy medical observers, forwarded to the secre-"tary of the American Public Health Association." Dr. Mac Clellan's paper is compiled from the personal recollections of medical practitioners in affected

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* Public Health : Reports and Papers presented at the Meetings of the American Public Health Association in the year 1873. New York, 1875.

localities, very soon after the subsidence of the disease, few, if any, of whom had kept, as he is careful to state, records, or had any notes of the cases they observed, made at the time of their occurrence. This imperfection of data greatly obscures the questions which have arisen concerning this prevalence of disease, in so far as the causes of its particular distribution in the basin of the Mississippi are concerned.

I had intended to have prepared a summary of the reports and papers contained in the volume of Transactions of the American Public Health Association referred to, and of the report of the Louisiana State Board of Health on the occurrence of "cholera" in New Orleans in 1873; but I have recently learned that a report has been prepared on the whole subject, under the authority of the United States Congress, and is about to be issued. As this report will no doubt supply the data which have hitherto been wanting, it will be sufficient for me here, with one exception, to direct attention to its near publication.

The exception relates to the first appearance of the choleraic disease at New Orleans. There appears to be a common consent in opinion, that the occurrences of the disease, in various localities along the course of the Mississippi, followed in a certain succession after the appearance of the malady in New Orleans. This is shown in some detail in Dr. Judson's report, and if the communications made to Dr. Mac Clellan are to be accepted, there can be little doubt that the successive appearances were due to successive infections. Opinions on this subject have, however, been very much governed by the notions entertained by different observers of the nature of the disease. How diversely this has been regarded is well illustrated by the certificates returned in the cases of death from it in New Orleans. The following nomenclature was indifferently employed by various practitioners: *Cholera morbus*,* *cholera spasmodica, cholera sporadica, cholera nostra, "apparently cholera," cholera Asiatica* (this latter term "infrequently"). It is admitted, however, that the disease designated by these several names was one and the same malady.

According to the *Annual Report of the Board of Health to the General Assembly of Louisiana*, 1873, (C. B. White, M.D. President,) "cholera," that is, the disease under consideration, appeared first in the United States in 1873, at New Orleans.† The history of each of the first 25 cases, it is stated, was submitted to careful inquiry as to importation, portability, and infectiousness, embracing all particulars with reference to contact with passengers or their baggage, the washing of clothes from persons on shipboard, &c. The particulars relating to these cases are given in some detail, but I do not repeat them here as they give no help in enabling a judgment to be formed as to diagnosis, and the results arrived at as to the causes determining them are stated with sufficient explicitness in the summary of the board's conclusions. The first death from the disease occurred on the 9th February, the last on the 21st February. Within that period the number of deaths registered from choleraic disease

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* The term *cholera morbus* is used in the following sense in the United States. "The term cholera," writes Dr. George B. Wood, (*A Treatise on the Practice of Medicine*, Art. *Cholera Morbus*, vol. i., p. 803,) "is given to any complaint in which "the prominent characters are simultaneous and repeated vomiting and purging, "with painful spasm of stomach and bowels, and occasional cramps of the external "muscles. Three varieties have been observed, so different in the circumstances of "their occurrences, as well as of their symptoms, progress, and results, as to merit "description. These are *cholera morbus, epidemic cholera*, and *cholera infantum*. "The present article is devoted specially to the first of these affections. It is the "variety so common as an endemic disease in various parts of the *United States* "during the summer season, and no doubt the same as that noticed by the ancient "authors, and described by Sydenham as occurring epidemically in England towards "the close of summer and beginning of autumn. By recent writers it is distinguished from the spasmodic variety by the name of *common* or *sporadic cholera*. " . . . . In persons of good constitution, the disease is very rarely fatal; it is "most apt to prove so in the very old, the feeble, and the intemperate."

† A summary of the portion of the report which relates to cholera is given in the volume of Transactions of the American Public Health Association for 1873. It appears to me desirable to put on record here certain portions of the original report.

in New Orleans, was 359. The distribution of the deaths in the several months of the year, arranged in three categories, is given in the following summary return:—

New Orleans, 1873.

	Cholera Sporadica.	Cholera Infantum.	Cholera Morbus.	Total.
January	—	—	—	—
February	3	—	1	4
March	4	2	8	14
April	28	17	36	81
May	97	50	39	186
June	9	15	9	33
July	—	16	3	19
August	—	3	1	4
September	—	3	2	5
October	—	6	—	6
November	1	4	—	5
December	—	2	—	2
Total	142	118	99	359

Eighteen other deaths from "cholera" are included in the return of the special investigation made into the origin of the disease by the Board of Health.

The following extracts from the report give the particulars which I am wishful to place on record here:—

"Of the first 25 cases, the white numbered eleven (11), colored fourteen (14).

"The population of New Orleans is estimated at 200,000, of which one fourth belongs to the African race, or is of mingled blood, so that if the races had been equally affected, the proportion should have been, say 6 colored to 18 whites.

"The mortality, throughout the prevalence of cholera, was at the rate of 10 blacks to 13 whites.

"The negro race, as is well known, suffer more severely from cholera than the white races.

"The multiple cases of the cholera record are:

"No. 5, Margaret Woods, „ 10, Isabella Woods,	535, Good Children Street	March 2nd. „ 8th.
„ 17, William Brady, „ 18, William Johnson,	S. B. Sabine - -	„ 30th. „ 31st.
„ 19, Sarah Jackson, „ 20, Henrietta Jackson,	146, Chartres Street -	„ 31st. April 1st.
„ 34, Joseph Stratmeyer, „ 46, Mrs. Stratmeyer,	Gentilly Road - -	„ 12th. „ 15th.
„ 49, Francisco, „ 55, Francisco, „ 56, Antonio,	238, Julia Street - -	„ 16th. „ 17th. „ 18th.
„ 64, Collin, „ 68, Allain,	10, Dumaine Street -	„ 22nd. „ 24th.
„ 79, O'Brien, Julia, „ 79, O'Brien, John,	308, Magazine Street -	„ 26th.
„ 158, Mr. Bire (recovered), „ 159, Lizzie Bire (died),	Cor., Julia and Delta -	May 14th.
„ 191, Colored woman, „ 226, Joseph Dolun, „ 253, Charles Ploff,	Insane Asylum - -	„ 20th. „ 28th. June 21st.

(pp. 30–31.)

. . . . . "The total number of cholera deaths, in the first six months of 1873, is two hundred and forty-four (244).

"During the same period, the cholera infantum deaths amounted to 85.

"As the average cholera infantum death rate for the first six months of five successive years is about forty (40), it is probably just to attribute the increase of the mortality this year to cholera sporadica, and estimate the total mortality by this last-mentioned disease at about three hundred (300).

"The disease occurred in nearly all parts of the city; yet, as usual in cholera epidemies, those living in the densely populated and unclean parts of the city suffered most.

"No suspicion of the existence of cholera in New Orleans having been aroused, and it not being unusual for fatal cases of congestive intermittent to be furnished with certificates of death by cholera, or cholera morbus, the first six cases were not called to the attention of the Board.

"The seventh occurred at the Charity Hospital, and official notice was given of its existence. The history of antecedent cases was, therefore, immediately looked up, and every subsequent case visited without delay, and its history carefully ascertained.

"Some discussion having arisen since that time as to the question of importation, the ground has again been carefully gone over, and the particulars of the cases whose history has been furnished, when practicable, minutely ascertained.

"These enquiries, as previously stated, embraced all modes of infection and importation, as by visiting ships, the washing of clothing for persons connected with shipping, visiting of sailor boarding houses, contamination of drinking water, &c. &c. This remark applies, not only to the 25 cases whose history is given in full, but to every case recorded.

"The statement has been made in many newspapers, and some scientific journals, that cholera was introduced into New Orleans by vessels from foreign ports, attention being specially directed to those of the Black and Baltic Seas. Through incorrect information, some notoriety was given to the statement that Odessa was the source and origin of all the evil.

"Examination of the records of the arrival of vessels demonstrates that from October 1st, 1872, to June 1st, 1873, no vessel came to New Orleans from Odessa, or any point on either the Baltic or Black Seas, and that the only arrivals with passengers from European ports, from January 1st, 1873, to May 1st, 1873, were from Liverpool and Newport, England; Hamburg, Bremen, Palerma, and Marseilles.

"All sick emigrants in charge of the Emigration Bureau are sent to pay wards of Charity Hospital for treatment. Foreign sailors are sent to this institution, and to the Hotel Dieu. No case of cholera occurred among emigrants. Two seamen of the English ship "Belgravia" were attacked with cholera, the one April 14th, and recovered; the other April 16th, and died the 17th.

"The 'Belgravia' left England January 29th, passed quarantine April 4th; her crew had therefore been 10 days in New Orleans, and 75 days out from Liverpool, before the appearance of the disease. Thirty-seven cases of cholera had occurred in New Orleans previous to the sickness of these seamen.

"These are the only two cases of cholera that occurred among or near to the shipping, or that had any connexion with it.

"Referring to the question of the introduction of cholera from foreign ports into New Orleans, Dr. Howe, resident physician at the quarantine station, Mississippi River, makes the following statement:—

"'C. B. White, M.D., President Board of Health,

"'New Orleans, La. Office of Quarantine Physician, Mississippi

"'Dear Sir, River, July 21st, 1873.

"'Yours of July 18th, making inquiry as to whether or not any vessel had passed the station since January 1st, 1873, on which there existed cholera, or upon which cholera had existed during the voyage and prior to arrival here, is just at hand.

"'Since January 1st, 1873, there have passed and been personally examined 638 vessels of all kinds, and in no instance has there been cholera in any form. Nor has there been, as far as I could ascertain, any cholera during the passage of any vessel to this port. My information has been, in every instance, obtained from the master of the vessel, as well as from the medical officer when there was one on board. In some instances, when vessels have arrived from ports

where cholera was supposed to exist, I have required a sworn statement from the master, signed by himself, which is kept on file as additional evidence. And in no instance have I had reason to doubt the truth of any statement or sworn affidavit.

" ' Attached and forming a portion of this report will be found an official list of infected vessels arriving here since January 1st, 1873, as well as of vessels detained in quarantine, with full particulars concerning cause of detention, number of sick removed, with disease and result.

" ' Any further information will be given with pleasure, while

" ' I remain, very respectfully,

" ' (Signed) George Howe, M.D.

" ' Resident Physician, Quarantine Station,

" ' Mississippi River.'

" From the facts and statements furnished, it is evident that the epidemic is singularly free from even the suspicion of importation," (pp. 32–34).

" . . . . The first deaths of cholera or cholera morbus occurred February 9th and 10th. On the 7th the range of temperature was 24·5 deg. F.; on the 10th 19·51 deg. F. It will be recollected that Surgeon Vickery, in his account of the second case, thought the unusual depression of temperature had much to do with its fatal result.

" The third death of cholera occurred February 28th. On the 24th, 25th, and 26th the ranges of temperature were respectively 18 deg., 19 deg., and 17 deg.

" During the first 10 days of March, nine (9) deaths occurred, accompanied by very considerable daily oscillations of temperature, the mercury ranging on one day 18 deg., on another 20 deg., and on two days 20·5 deg.

" The months of March and April throughout present remarkable daily ranges of temperature.

" It seemed pretty evident that in many cases the exciting cause of the attack was sudden, and considerable change of temperature. . . . .

Table showing Variations of Temperature in New Orleans during the Six Months ending June 30th, 1873.

Month.	Daily Range, ° F.			No. of Days over 20° F.	No. of Days over 14° F.	No. of Days over 8° F.
	Highest.	Lowest.	Mean.			
January -	23·5	5·0	12·76	2 days.	10 days.	27 days.
February -	24·5	7·5	15·59	3 „	15 „	27 „
March -	37·0	7·5	16·17	7 „	19 „	29 „
April -	30·5	6·0	16·06	5 „	20 „	27 „
May -	21·0	9·0	14·29	1 „	14 „	31 „
June -	20·0	5·5	13·38	—	7 „	28 „
	—	—	14·66	18 days.	85 days.	169 days.

" April and May are the diarrhœa months of New Orleans. The attacks are seldom severe, and in most cases yield immediately to a very moderate dose of some mercurial, with or without opiates or astringents.

" This too is the cholera infantum period of the year in New Orleans. Our small mortality from that disease occurs almost entirely in the first half of the year.

" The comparative exemption of New Orleans is probably in a considerable degree attributable to the evenness of our summer temperature.

" The summer thermal lines given in the last report of the Board of Health of New Orleans afford an interesting comparison with those of the Board of Health of New York for the same period.

" In calling attention to rainfall, as exhibited in the chart farther on in the report [not printed with this extract], it is to be remembered that in

1873 April and May, meteorologically, seemed to have changed places. April is usually a showery month, and May almost unvaryingly pleasant; literally a month of sunshine.

" The chart shows April of 1873 very dry, and May a month of heavy and repeated rainfalls. In New Orleans one half inch of rainfall is only an ordinary shower, whose effect immediately disappears, unless it has been preceded by others.

" With the high, cool, and dry winds prevailing, the whole city, during the month of April, was enveloped in clouds of dust [which appears to be particularly foul from decomposing organic matter].

" Several days entirely without fall of rain preceded the appearance of the first cases of cholera in February, and again preceded the first cases in March.

" There is a general coincidence between the occurrence of cholera cases and the lack of rainfall, which is more noticeable by the table of cases than on the chart, as lines of the latter are drawn to show deaths by weeks.

" New Orleans should be free from contagion of drinking water by cholera poison, as usually caused, because of its water supply.

" The larger portion of its inhabitants drink rain-water from cisterns, which are invariably above ground. The remainder drink hydrant water from the Mississippi. Water from wells is never used for cooking or drinking." (pp. 36–39). . . . . " Of the first 80 deaths, 46 received certificates of death by cholera morbus.

" Even at this time [December 1873] the opinion of the physicians of New Orleans is divided upon the subject.

" Medical men connected with hospitals, seeing few save fatal cases, unhesitatingly pronounce the disease Asiatic cholera.

" A large portion of New Orleans physicians consider it not to have been Asiatic cholera; all, however, agreeing that in fatal cases no distinction can be drawn between the cholera sporadica of 1873, at New Orleans, and genuine Asiatic cholera.

" The few holding that when no distinction exists there is no difference, unhesitatingly pronounce the disease Asiatic cholera, and suggest that importation is not necessary, that the germs of that disease are always and everywhere present, only awaiting favorable circumstances to multiply and produce the effects customarily experienced from the general and abundant presence of cholera poison.

" Most physicians, however, although admitting the difficulty of differential diagnosis in fatal cases, consider that the character of the disease, its course and progress as a whole, warrant the belief that it was not Asiatic cholera.

" Some of the considerations influencing them to such belief are :—

" 1. The non-importation of the disease.

" 2. That no evidence of portability or infection was exhibited in the city, where every facility existed for ascertaining its natural history.

" 3. The appearance of the disease at many localities remote from each other, and from anything that could be considered a common cause, and in all parts of the city, at dates synchronous or nearly so.

" 4. The small mortality of those attacked with vomiting and purging during the presence of the disease, attacks similar to which, during the presence of former epidemics, have customarily proved the beginning of that usually fatal disorder.

" The death-rate of persons thus attacked is variously estimated at from 3 to 12 per cent..

" 5. The fact that so general diffusion of the disease existed without resulting in a great epidemic.

" Had the disease possessed the portability and infectiveness attributed to Asiatic cholera, its course and results would have been the reverse of the actual occurrences.

" 6. The fact of the long-continued presence of the disease in New Orleans, without flaming up to epidemic proportions, shows absence of the peculiar characteristics of Asiatic cholera, as generally admitted.

" The disorder seemed endemic, not epidemic.

" 7. Cholera occurred at the season of the year when intestinal disorders appear in New Orleans, April being the diarrhœa month of the year.

" The city's small mortality of cholera infantum occurs also in the first half of the year.

" The prevalence of cholera at the same period of 1873, may be viewed as the natural tendency of that portion of the year, exaggerated into serious and deadly, and somewhat general disease, by the presence of local poison, engendered by filth and magnified by unusual meteorological conditions.

" 8. The amenability to treatment of what were in appearance serious cases.

" Under the hypodermic use of morphine and atropia, or morphine alone, immediate relief and ultimate recovery was the rule; under treatment by calomel and quinine, recovery also seemed speedy; also, under domestic remedies, many cases were restored to health.

" A large number of persons were taken ill with profuse vomiting and purging, sometimes preceded by faintings and cramps, with great subsequent weakness, who recovered without any aid whatever, save the vis medicatrix naturæ.

" 9. The small number of multiple cases is considered an evidence of its non-infective or epidemic character.

" 10. The disease was not carried to our neighbours.

" With Mobile, constant intercourse continued at the rate of two passenger trains per day, each way, with numerous freight trains, and to the hamlets along the Mississippi Sound, three trains per day each way.

" Neither in these small villages nor in Mobile did cholera occur." (pp. 42–44.)

A copy of the report called for by Congress, on the cholera epidemic of 1873, in the United States, reached me as the present report was about to go to press.* This report forms a large octavo volume, and it is divided into two parts, each paged separately. The first part, of 28 pages, contains a report by Dr. John M. Woodworth, supervising surgeon, U.S. (merchant), Marine Hospital Service, on "The Introduction of Epidemic Cholera through the Agency of the Mercantile Marine: Suggestions of Measures of Prevention." The second part, of 1,025 pages, contains a series of three reports, namely, (A). *A history of the Cholera Epidemic of* 1873 *in the United States*, by Dr. Ely McClellan, assistant surgeon, U.S.A.; (B.) A *History of the Travels of Asiatic Cholera* (including much matter respecting previous epidemics of cholera in the United States), by Dr. John C. Peters, of New York City, and Dr. Ely McClellan; and (C.) *A Bibliography of Cholera*, by Dr. John S. Billings, assistant surgeon, U.S.A.

Dr. McClellan, in his account of the clinical history of the epidemic of 1873, expresses himself as fully satisfied that the disease was *malignant epidemic cholera*. The further inquiry as to the beginning of the epidemic in New Orleans was carried out by assistant surgeon Van Buren Hubbard, U.S.A. The following are extracts from his report of the results of this investigation, dated January 30th, 1874.

Referring to Dr. George Howe's letter, printed above, Dr. Van Buren Hubbard observes:—

" The tone of this extract is positive, and the evidence seemingly conclusive. Desiring, however, additional facts, upon August 5th, 1874, we addressed a letter to the quarantine physician of the Mississippi station, from which letter we make the following extracts:—

" I. Will you inform me if, during the months of December 1872, and January and February 1873, the quarantine upon the Mississippi river was rigidly enforced?

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* War Department, Surgeon-General's Office. *Cholera Epidemic of* 1873 *in the United States*. Washington, Government Printing Office, 1875.

"II. If during the months named any vessel from supposed infected ports (in original letter, ports were enumerated) arrived at the quarantine station upon the Mississippi river?

"III. If vessels from any of the ports named arrived at the Mississippi quarantine station, I would respectfully ask information as to the character of the inspection to which they were subjected."

"In answer to these questions, we received from Dr. A. W. Perry, late quarantine physician of the Mississippi river station, a communication dated August 21st, 1874, of which the following is extracted: "*Quarantine in the months you refer to was confined to asking each captain the questions I here enclose.*" We reproduce the list of questions:—

Number of permit?	Number of passengers, foreign?
Date?	Number of passengers, domestic?
Name of tow-boat?	Where are passengers from?
Kind of vessel?	Any sickness while out?
Name?	What kind?
Name of master?	Any deaths?
Name of pilot?	What cause?
Where from?	Are all well now?
Number of crew?	Have you a bill of health?
Kind of cargo?	Number of days out?

"The letter of Dr. Perry further contains a list of 175 vessels that arrived at New Orleans during the three months named, bringing into that port from the localities before alluded to 1,844 passengers and 3,500 of crew, a total of 5,344 individuals, the majority of whom were from localities suspected of cholera.

"From an examination of the monthly reports of the Mississippi Quarantine Station, which were furnished through the kindness of the president of the Board of Health, the following tables have been prepared:

"I. A tabular statement of the number of vessels, with the number of passengers and the number of crew, that arrived at the port of New Orleans, La., during the month of December 1872, and the first six months of 1873.

Month.	Number of Vessels.	Number of Passengers.	Number of Crew.
December 1872 - - -	150	2,204	2,684
January 1873 - - -	134	1,169	2,667
February 1873 - - -	100	550	1,884
March 1873 - - -	118	726	2,254
April 1873 - - -	121	804	2,285
May 1873 - - -	86	708	1,592
June 1873 - - -	60	406	1,365
Total - - -	769	5,163	14,731

A grand total of 15,294 individuals.

" II. A tabular statement of the number of vessels, with the number of passengers and the number of the crew, that arrived at the port of New Orleans, La., during the month of December 1872, and the first six months of 1873, from European, West Indian, and South American ports.

Month.	Number of Vesssels.	Number of Passengers.	Number of Crew.
December 1872 - - -	68	1,407	1,145
January 1873 - - -	53	820	1,523
February 1873 - - -	41	278	823
March 1873 - - -	65	453	1,187
April 1873 - - -	57	491	1,240
May 1873 - - -	31	481	669
June 1873 - - -	27	329	662
Total - - -	342	4,249	7,249

A grand total of 11,498 individuals.

" Following further this line of investigation, from the Annual Report of the Commissioners of Emigration for the State of Louisiana, we quote the following:

Statistics of Immigration.

" The number of foreign immigrants arrived at the port of New Orleans during the year ending December 31, 1873, is as follows:

From Bremen - - - - - - -	2,938
From Hamburg - - - - - - -	576
From Liverpool - - - - - - -	1,834
From Bordeaux - - - - - - -	151
From Havre - - - - - - - -	239
From Marseilles - - - - - - -	6
From Palermo - - - - - - -	121
From Messina - - - - - - -	3
From Genoa - - - - - - - -	1
From West Indian and South American ports - -	210
Total - - - - - -	6,079

" 5,687 arrived in steamships, and 392 in sailing vessels. (pp. 106–108.)" . . .

" . . . . Of this number (6,079) 4,122 were males, 1,957 were females.

Through the kindness of Mr. H. Von Werthen, the agent of the emigration bureau, we obtained much valuable information as to the emigrants who arrive at the port of New Orleans, and from the facts thus obtained we are able to present the following table:

" A tabular statement as to the number of emigrants who arrived at the port of New Orleans, La., during the month of December 1872, and the first six months of 1873, with the port from which they sailed for the United States.

Port of Departure.	December.	January.	February.	March.	April.	May.	June.	Total.
Liverpool - - -	467	424	65	190	112	94	244	1,596
Hamburg - - -	491	—	—	91	109	—	—	681
Bremen - - -	417	169	153	53	224	345	—	1,361
Barcelona - - -	2	—	—	—	—	—	—	2
Marseilles - -	3	—	—	—	—	—	—	3
Bordeaux - - -	11	—	—	—	—	3	—	14
Havana - - -	8	3	15	18	8	11	9	72
Vera Cruz - - -	—	—	3	26	—	32	—	61
Palermo - - -	—	—	—	114	6	—	2	122
Totals - -	1,399	596	236	482	459	485	255	3,912

" Prior to the outbreak of cholera at New Orleans, it was an ascertained fact that cholera was upon its westward march, and that the disease had already, in one instance at least, reached the shores of North America. On the 6th November 1871, the steamship " Franklyn," from Stettin, arrived at Halifax, having had an outbreak of cholera on the voyage. Two men from the shore who were employed, after her arrival, on this steamer, were taken with cholera.

" One died of the disease at his home in Halifax, the other man, after he became sick, went to his home at Chezzetcook, a small fishing-village twenty-two miles south-east of Halifax, and there died. At Chezzetcook four other cases occurred in the family of this man (Lepiere) two of which were fatal.

" The most efficient sanitary precautions were at once adopted at Halifax, and no other cases occurred. After it was known that the disease had been carried to Chezzetcook, the Government adopted stringent sanitary measures, and at once checked the spread of the disease.

" During the series of inspections instituted at New Orleans during 1874, it was several times intimated to us, by sanitary observers, that cholera existed in the West Indies during the late months of 1872, but that the fact of its existence had been suppressed. We have most carefully investigated this matter, without, however, obtaining any very definite results. The only clue that could be found was obtained through the supervising surgeons of the marine hospital service, who furnishes us with a letter of the honorable the Secretary of State, from which the following extract is made :—

" Under date of September 23, 1872, the consul at Kingston, Jamaica, reports the arrival of a coolie ship at Bluff's Bay in that island, and that one case of cholera had occurred since the arrival, resulting in the death of one of the coolies. It was reported also that some sixty of the coolies died on the passage, but the disease was not ascertained by the consul.

" The list of the vessels that arrived at the port of New Orleans during January, 1873, shows that direct communication was established between that city and Jamaica and the adjacent islands. January 21, 1873, the schooner " Mai " arrived from Port Antonio. January 24, 1873, the schooner " Challenger" arrived from Grand Cayman.

" The facts which have thus far been obtained go to prove :—

" I. That prior to the outbreak of cholera at New Orleans, in 1873, a coolie ship infected with the disease had arrived at Jamaica; and that after her arrival at least one cholera death had occurred on that island.

" II. That at the Mississippi river quarantine, during the last month of 1872, and the early months of 1873, the only inspection to which vessels arriving at that station were subjected, consisted in receiving as final the answers which the officers of vessels saw fit to make to an imperfect list of questions.

" III. That during the months named a large number of emigrants arrived at the city of New Orleans from cholera-infected districts.

Upon pushing the investigation further, we are informed that the Commissioners of Emigration exercise no control over emigrants who arrive at the port

of New Orleans, other than of an advisory nature. That the effects of emigrants are inspected upon ship-board by a customs' officer, and that upon landing the emigrant follows unmolested his personal inclinations. That the large majority of the emigrants who arrived at the port of New Orleans, in the month of December, 1872, went at once to the state of Texas, but that during the succeeding months large numbers passed into the interior of the United States by the Mississippi river route. Emigrants for Texas are usually shipped direct by the Morgan line. The depôt of this company joins the ship and the steamboat levee; and individuals availing themselves of this route are seldom detained over night at New Orleans.

" Emigrants who desire to pass northward by the Mississippi river remain sometimes for days in the city, *and lodge at emigrant boarding-houses, which face the river upon the steamboat levee. It is an ascertained fact that during the months of January, February, and March many of these houses were filled with individuals of this class.*

" We have, therefore, traced individuals from cholera-infected districts of Europe directly to that locality of the city of New Orleans at which the report, of the Board of Health states the earlier cases of the disease became infected.

" The evidence, although circumstantial, is certainly strong that the unfortunate individuals who contracted cholera upon or near the steamboat levee came in contact with the poison which had been imported in the effects of emigrants from the cholera-infected districts of Europe, from which infected districts it is shown that emigrants did arrive prior to the occurrence of the initial case in the city of New Orleans. This is certainly more reasonable, more in accordance with history, than it is to suppose that a *de novo* development of Asiatic or epidemic cholera occurred at the beautiful crescent city.

" The doctrine of " non-importation " will not stand.

" We fully admit that by the board of health, whose officials were earnest in the endeavour to discover the arrival of individuals who might be infected with cholera, every effort was made to develope the facts attending the introduction of the disease. We have with the greatest care gone over the ground which had been previously investigated by the President of the Board of Health, and have been able to determine three additional facts :

" I. The arrival of a cholera-infected ship at Jamaica in September 1872, and the fact that at least one case of the disease occurred upon that island after the arrival of the ship.

" II. The utterly worthless and unreliable quarantine which was maintained at the Mississippi river station during December 1872 and January and February 1873. It must be remembered that this station is on the Mississippi river, at a very considerable distrance below the city of New Orleans, and therefore far removed from the direct control of the Board of Health.

" III. The arrival of emigrants from cholera districts, and the location of such emigrants at the very point in the city of New Orleans at which the early cases of the disease occurred.

" It is submitted that these facts destroy utterly the theory of the original development of cholera in 1873 in the United States." (pp. 109–111.)

Note D.

Note on Cholera in East Africa, 1870–71.

Since the completion of this Report, Dr. Christie has favoured me with the following note, containing additional information relating to the progress of Cholera in East Africa in 1870–71 :—

Cholera appeared at Mozambique, as previously stated, on May 6th, 1870, and, according to native report, the tract of the epidemic was from the interior of Africa. This is exceedingly probable for at that time there was no report of the disease on the coast further south than Cape Delgado, and it would be impossible, in the month of May, for any native craft, or even square-rigged vessel, to make Mozambique from the north against the S.W. monsoon. The probability is that it reached Mozambique from the south of Tanganyika by

means of the Wabisa, who are the middle men of the inland traffic. Mozambique infected Majunga, on the north-west of Madagascar, in the month of August 1870, and the island of Johanna on the 16th August, doubtless by means of slave dhows in both cases.

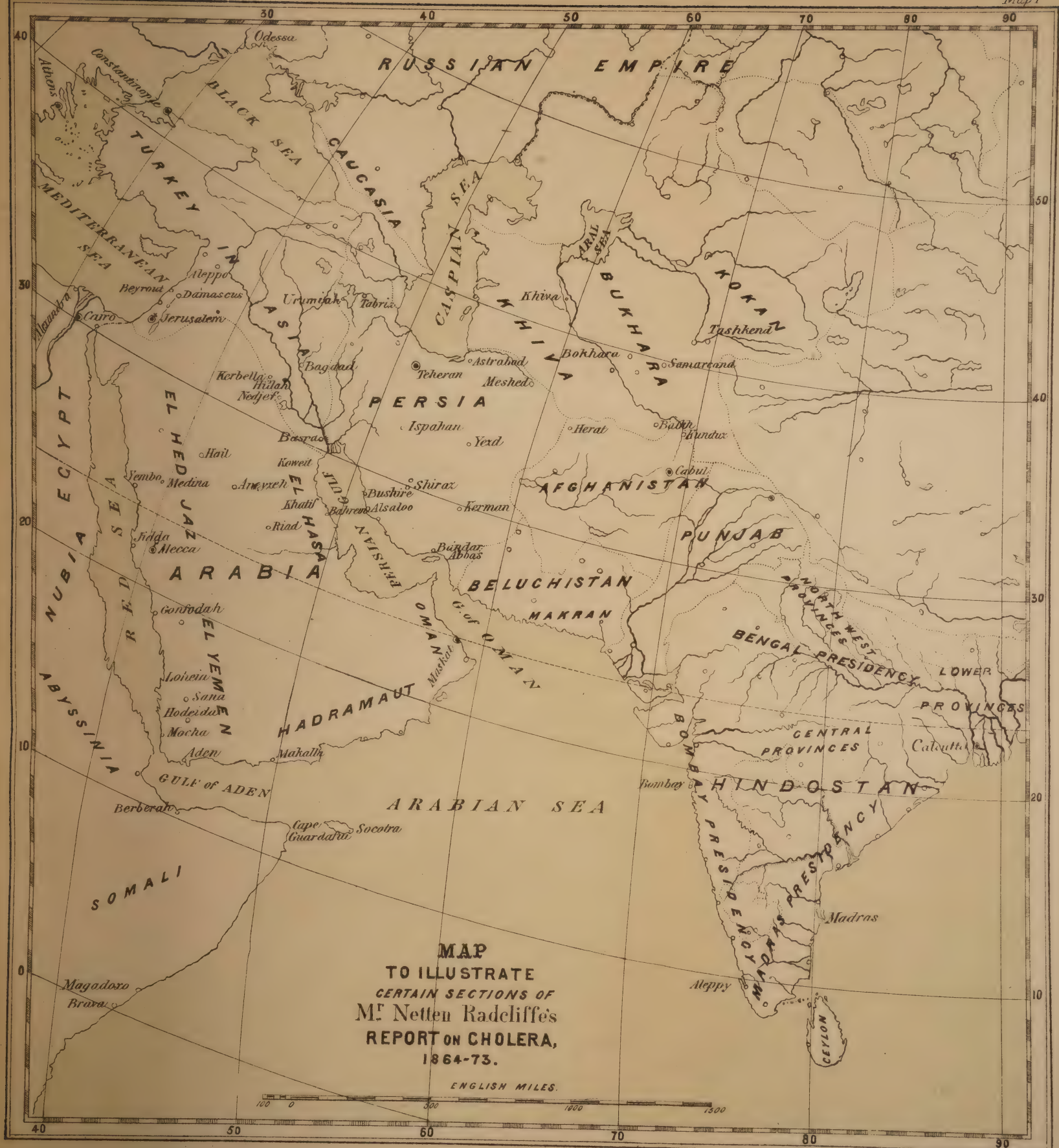
"At Majunga the mortality was very great and two Bahoras, natives of India, died. To what extent the disease spread in the interior I am not aware. Nossi Bey was infected by Majunga in September 1870, and a second time in March 1871.

"In Johanna the disease continued from 16th August till October, and the island was infected a *second* time on December 14th, but this time the disease was conveyed from Nossi Bey, and it continued in Johanna till the 2nd January, 1871. There were 378 deaths. The disease was principally confined to the town. All communications between the town and the sugar estates of the Sultan and Mr. Sunley was stopped, and there were no deaths there. Dr. Morton of H.M.S. 'Wolverine' collected for me the facts regarding Johanna shortly after the close of the epidemic, when the 'Wolverine' visited the island.

"Mozambique infected Ibo on the 11th January 1871, and Quilimane in February of the same year. The facts regarding Ibo are as previously narrated. At Quilimane the mortality was very great, and amongst the natives it was estimated that from four to five thousand died, and the disease was still there at the end of May 1871. At the time there was a large force in readiness to proceed up the Zambezi against the rebel chief Bonga, but one third having perished from cholera the expedition for the time had to be abandoned. The disease passed into the interior and further trace of it was lost. The progress of the disease from Zanzibar to the northern ports may be shortly stated. The dhows for the north began to leave early in April 1870, and every harbour in communication with Zanzibar was infected as far north as Socotra.

"Mr. Heale sailed from Zanzibar for Brava in a dhow on the 16th April. On the second day after the dhow reached Brava the disease appeared there, and continued for two months. It was reported that half the population perished. Mr. Heales' estimate of the deaths among the Somalis was 200, but the mortality was great among the negroes. The dhow passed on to Aden, carrying letters for Zanzibar which were received at that place on July the 18th.

"It is possible that the disease may have been carried to Makalla or the Persian Gulf, crossing the tract of the epidemic, in May 1870, which entered Africa in November 1864. Socotra, the last place to the north where further trace of it is lost, cannot be far from the line of the track of entrance, five and a half years before."



Dangerfield, Lith., 22, Bedford St. Covent Garden.

CHOLERA, 1864-65.
MAP SHOWING DISTRIBUTION IN WESTERN DIVISION OF EASTERN HEMISPHERE.
DISTRICTS OF PREVALENCE.
30 20 10 0 10 20 30 40 50 60 70 80
60 50 40 30 20 10 0 10 20

Dangerfield, lith. 22 Bedford St. Covent Garden.

CHOLERA, 1866.
MAP SHOWING DISTRIBUTION IN WESTERN DIVISION OF EASTERN HEMISPHERE.
DISTRICTS OF PREVALENCE.
30 20 10 0 10 20 30 40 50 60 70 80
60 50 40 30 20 10

CHOLERA , 1867.
MAP SHOWING DISTRIBUTION IN WESTERN DIVISION OF EASTERN HEMISPHERE.
DISTRICTS OF PREVALENCE.
30
20
10
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30
40
50
60
70
80
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50
40
30
20
10

CHOLERA, 1868.
MAP SHOWING DISTRIBUTION IN WESTERN DIVISION OF EASTERN HEMISPHERE.
DISTRICTS OF PREVALENCE.
30 20 10 0 10 20 30 40 50 60 70 80
60 50 40 30 20 10 0 10 20

Dangerfield, Lith. 22, Bedford St. Covent Garden

CHOLERA, 1869.
MAP SHOWING DISTRIBUTION IN WESTERN DIVISION OF EASTERN HEMISPHERE.
DISTRICTS OF PREVALENCE
30 20 10 0 10 20 30 40 50 60 70 80
60 50 40 30 20 10 0 10 20

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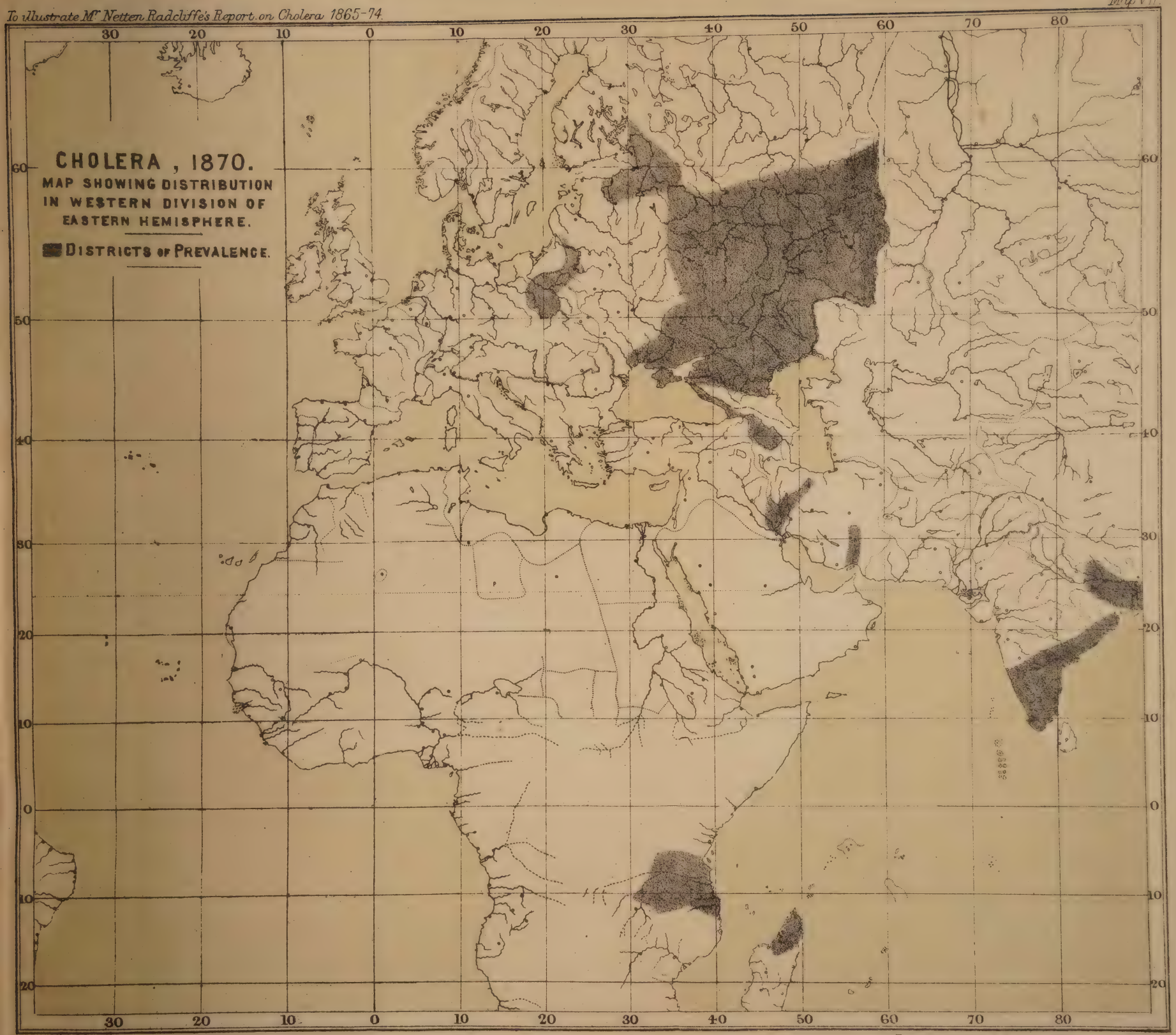
To illustrate Mr Netten Radcliffe's Report on Cholera 1865-74.


CHOLERA, 1870.
MAP SHOWING DISTRIBUTION IN WESTERN DIVISION OF EASTERN HEMISPHERE.
DISTRICTS OF PREVALENCE.
30 20 10 0 10 20 30 40 50 60 70 80
60 50 40 30 20 10 0 10 20

Dangerfield, Lith. 22 Bedford St. Covent Garden.

CHOLERA, 1871.
MAP SHOWING DISTRIBUTION IN WESTERN DIVISION OF EASTERN HEMISPHERE.
DISTRICTS OF PREVALENCE.
30 20 10 0 10 20 30 40 50 60 70 80
60 50 40 30 20 10 0 10 20

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Dangerfield, Lith. 22, Bedford St. Covent Garden.

No. 2.—Abstract by Dr. Seaton of Proceedings of the International Sanitary Conference held at Vienna, July 1 to Aug. 1, 1874.

The International Sanitary Conference of Vienna, to which I had the honour of being delegated, along with Dr. Dickson of Constantinople, as representing the United Kingdom, was assembled at the instance of the Austro-Hungarian Government for objects which are stated at length in the dispatch of Count Andrássy, appended to this paper (Annex I.). Summarily, these objects were (1) to re-examine the state of our knowledge of cholera in reference to prophylaxy, with the view of establishing, if possible, a complete understanding between the Governments who had been convoked as to the national and international measures to be adopted for preventing the spread of that disease, "de concerter entre les États "intéressés des arrangements obligatoires qui auraient pour but "d'amener une parfaite conformité dans les dispositions à prendre pour "se prémunir contre ce danger commun;" and (2) to consider the question of instituting a permanent, or temporary, international sanitary commission for the further investigation of epidemics and the means of combatting them. It was reserved for the Conference to enter or not, as it might see fit, on the subject of quarantine against other diseases than cholera.

Every European State was represented at this Conference. Persia and Egypt were also represented. The United States of America had been invited by the Austro-Hungarian Government, and had accepted the invitation, but no representatives attended. The States represented were 22 in number,* each sending as many delegates as it thought fit, but each disposing of one vote only. The delegates were, with few exceptions, of the medical profession, and no State was without a medical representative. Most of the delegates were persons holding office in the public service, sanitary or medical, of their respective countries.

The Conference was formally opened July 1st, 1874, and formally closed August 1st, 1874. During this time 20 sittings of the full Conference were held, independent of the meetings of the several committees to which had been entrusted the preliminary consideration, and preparation for discussion, of some of the more important questions on which the Conference had to decide.

Following the programme which had been proposed and submitted to the respective Governments in Count Andrássy's despatch (Annex II.) certain preliminary scientific questions in reference to cholera were first submitted for consideration. These the Conference decided to consider in full assembly without the intermedium of committees. As most (though not all) of these questions had been thoroughly discussed by the Conference which had been held eight years previously at Constantinople, it was determined, in order to facilitate business, that as each such question arose the conclusions arrived at on the subject by the Constantinople Conference should be read, and a provisional vote thereon taken without discussion. If the result were one of unanimous assent, the question was regarded as settled in that sense, and the Conference passed on to the next question. But if the assent were not unanimous, if a single delegation of those present at the particular time even abstained from voting, the discussion was declared open. This mode of proceeding was found in practice extremely convenient and led to a great saving of time.

* Austria, Hungary, Belgium, Denmark, Egypt, France, Germany, Great Britain, Greece, Holland, Italy, Luxembourg, Norway, Persia, Portugal, Roumania, Russia, Servia, Spain, Sweden, Switzerland, Turkey.

I.—Scientific Questions.

The first of the preliminary questions was as follows :—"Le choléra "Asiatique, susceptible de s'étendre (épidémique), ne se développe-t-il "spontanément que dans l'Inde, et est-ce toujours du dehors qu'il "arrive quand il éclate dans d'autres pays? Ou bien revêt-il aussi le "caractère endémique dans d'autres pays que l'Inde? dans ce cas, quels "sont ces pays ?"

On the points involved in this question the Conference was in unanimous agreement with that of Constantinople, that epidemic cholera has its origin in India, and exists permanently there in an endemic state; that it is probably endemic *only* in India, though there are some countries bordering on India, concerning which sufficient grounds do not exist for a formal conclusion on this point; that it has never been observed in a really endemic state, (which of course must be carefully distinguished from an origin from secondary foci) either in any part of Europe, or in Turkey in Asia, or in the Caucasus, or in the north of Africa, or in America; and that, though the possibility of its becoming acclimatized in any of those countries is not to be rejected, such event is to be held as extremely problematical.*

On the second question, "Le choléra est-il transmissible par l'homme ?" some discussion took place, not in reference to the main question, in which the Conference was entirely in accord with that of Constantinople, but on an exception taken by the German delegates to the wording of one of the conclusions of the Constantinople Conference on the subject.† With certain qualifications to meet this view, and which recognised the influence of localities, the Conference accepted those conclusions, thereby affirming that cholera is transmissible by the human subject coming from an infected locality; that the rapidity of its transmission is in correspondence with the activity and rapidity of human communications; that the introduction of a single cholera patient may give rise to the development of an epidemic; and that there are facts which tend to prove that a single individual (and *à fortiori* several) coming from an infected place, and affected with diarrhœa only, may be enough to give rise to the development of an epidemic of cholera, or, in other words, that the premonitory diarrhœa of cholera may be the means of transmitting the disease.‡

On the points raised in the third question, "Le choléra peut il être

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* Throughout this abstract I have given *in full* the conclusions as voted by the Conference. They frequently go beyond a mere categorical reply to the questions asked, and sometimes contain qualifications of the conclusions stated in the final "Relevé des Conclusions, &c." (Annex. III.) which should not be disregarded.

† The phrase objected to was "L'homme atteint de choléra est par lui-même le "principal agent propagateur de cette maladie." And the objection taken by Professor Pettenkofer was particularly to the words "par lui même." The view of the German delegation was thus formulated by Professor Hirsch :—"Je ne conteste "nullement la transmissibilitée du choléra par l'homme venant d'un milieu infecté; "je considère l'homme seulement comme la cause spécifique, en dehors de l'influence "de la localité infecté; en outre, je le considère comme le propagateur du choléra, "lorsqu'il vient d'un endroit où le germe de la maladie existe déjà."

‡ It is apparently by an error, which escaped observation at the time, in the Procès-verbaux, that the proposal of the German delegation is therein stated to have been formally adopted, and to the exclusion of the Constantinople resolutions. But the fact was that the discussion showed that there was nothing really to dispute about; the conference readily and at once recognized the influence of localities, and most certainly the resolutions of Constantinople, modified on this point only, as I have stated in the text, were adopted. I find this error in the Procès-verbaux and Relevé des Conclusions, has been since noticed by other Members of the Conference. (See Bull. de l'Acad. de Med. 1874, p. 926.)

" propagé par des effets qui, provenant d'un lieu infecté, ont servi à " l'usage, et spécialement par ceux qui ont appartenu à des cholériques ?" the conclusions of the Constantinople Conference were unanimously accepted, viz., that cholera is transmissible by goods employed for personal use coming from an infected place, and especially by such as have been used by cholera patients; and that there are even facts which show that the disease may be conveyed to a distance by such goods, if they have been kept close and unexposed to free circulation of air.

The fourth question, " Le choléra peut-il-être propagé par des comestibles ? " was one which had not been considered at Constantinople. This question it was decided after a short discussion to divide into two, the one having reference to food, and the other to drink, especially to drinkable water. To the first branch of the question, " Le choléra peut-" il-être propagé par les aliments ? " the answer given by a majority, after considerable discussion, was that the Conference having no conclusive facts of the transmission of cholera by food, was not in a position to give a formal decision on the point. To the second division of the question, " Le choléra peut-il-être propagé par des boissons, particulière-" ment par l'eau ? " the reply was unanimously in the affirmative.

On the fifth question, " Peut-il-être importé par des animaux vivants?" the conclusion arrived at by a majority, after some discussion, was that there exists no proof of the transmission of cholera from animals to mankind, but that the possibility of it may reasonably be admitted.

On the sixth question, " Le choléra peut-il-être importé par les " marchandises? " the conclusion of the Conference at Constantinople, that, while they were unanimous as to the absence of any proof of the transmission of cholera by merchandise, they must admit the possibility of such occurrence under certain conditions, was, after discussion, adopted by a majority. No vote was given against it, but several delegations abstained from voting. As is evident from the wording of the resolution, it was only as to the concluding phrase that there was any difference of opinion.

On the seventh question, " Le choléra peut-il-être propagé par les " cadavres des cholériques ? " the conclusion of the former Conference, that though there was no conclusive evidence of the transmission of cholera by the corpses of cholera patients, it was prudent to consider them as dangerous, was unanimously adopted.

On the eighth question, " Le choléra peut-il se propager au loin par " l'atmosphère seule ? " the Conference adopted, with equal unanimity, the conclusions of that of Constantinople, which were as follows: No fact up to the present time has shown that cholera can be propagated to a distance by the atmosphere alone, whatever the atmospheric conditions may be; and it is further a law, without exception, that no epidemic of cholera has ever been propagated from one point to another in a shorter time than was requisite for a human being to travel from the one point to the other. The surrounding air is the chief vehicle of the cholera-producing agent, but the transmission of the disease by the air is limited, in the immense majority of cases, to a distance very close to the source of infection. None of the facts which have been cited of transport of cholera by the atmosphere to the distance of one or of several miles is sufficiently conclusive.

The Conference assented also with unanimity to the answer which had been given at Constantinople to the ninth question, viz. " L'air frais " arrivant du dehors aux agents donnant naissance ou propageant le " choléra, et les aërant, ou bien l'isolement de ces agents de l'air extérieur, " constituent-ils des éléments ayant ou non une influence sur le caractère " contagieux du choléra ? " This reply was to the effect that in fresh air

the generative principle of cholera rapidly loses its morbific activity, but that under special conditions of confinement of air such activity might be preserved for an undetermined time; that it was under these conditions of confinement of air that, (as already stated in reply to question 3), cholera might be transmitted even to a distance by goods employed for personal use; that great deserts were a very efficacious barrier against the propagation of cholera, and that there was no example of that disease having ever been imported either into Egypt or Syria across the desert by caravans coming from Mecca.

The two remaining preliminary questions of the programme gave rise to long and animated discussions.

Question 10 was, "Quand il y a contagion, quelle est la durée de "l'incubation?" The resolutions of the Constantinople Conference on this point had been as follows:—"In almost all cases, the period of "incubation, *i.e.*, the time which elapses between the moment at which "the individual receives the cholera infection and the commencement of "the premonitory diarrhœa, or of the confirmed cholera, does not exceed "a few days [elsewhere more precisely limited by the words, 'a week "at the outside.'] All facts which have been cited of a longer "incubation relate to cases which are inconclusive, either because the "premonitory diarrhœa has been included in the period of incubation, "or because the infection might have taken place after the person's "departure from the infected locality. Observation shows that the "duration of the choleraic diarrhœa which has been termed premonitory, "(which must not be confounded with every diarrhœa met with at "cholera times), does not exceed a few days. The facts which have "been cited as exceptional do not prove that the cases of diarrhœa "prolonged beyond this period are really choleraic, and are susceptible "of transmitting cholera when the individual suffering has been with-"drawn from all sources of infection." After a very long debate, the Conference of Vienna assented to these conclusions by 13 affirmative votes to 1 negative, four delegations abstaining from voting.*

The 11th and last question was this:—"Connâit-on des moyens ou des "procédés de désinfection grâce auxquels le principe générateur ou con-"tagieux du choléra peut sûrement ou avec quelque chance de succès être "détruit ou perdre de son intensité? Dans le cas affirmatif, quels sont "ces moyens?" A short preliminary discussion made it evident that it would be desirable to take separately the opinion of the Conference as to the existence of means of disinfection which might be relied on with certainty, or only of means for the probable success of which there was good evidence; to separate, in short, the "sûrement" from the "quelque chance de succès." The known existence of any means of disinfection, absolutely certain in its operation, was denied by 12 delegations, and affirmed by none, seven delegations abstaining from voting.

* The difference of opinion, at least between the delegations which voted in the affirmative and those which abstained from voting, was, I apprehend, more apparent than real. I did not gather from the discussion that it was at all disputed by the latter that in the immense majority of cases (perhaps the expression "almost all" might have been felt by them a little too strong) the period of incubation does not exceed the limits stated in the resolution. Their objection attached rather to the too small importance, which, in a prophylactic point of view, the resolution seemed to attach to the exceptional cases, of which the most reasonable explanation consisted in admitting a longer period of incubation. As Professor Pettenkofer put it, the question was to be regarded from a prophylactic not a clinical point of view; adding, that from the latter "il accepterait la thèse d'une courte durée." On the other hand it was by no means intended, as the limiting word "almost" shows, by those who supported the resolution to deny the possible, nor the probable, existence of a longer period of incubation in some cases, nor that dangers might, though rarely, arise therefrom.

On the other hand 14 delegations asserted, while four denied,* the existence of means of disinfection, of the successful application of which there was reasonable probability. The vote on this latter question, however, must be interpreted by reference to a further discussion to which it gave rise, which showed that the objection on the part of the delegations which had voted in the negative, to admit the probable efficacy of disinfectants, had arisen chiefly, or at least in great part, from the influence they conceived an affirmative answer to the question would have in leading to a reliance being placed on disinfectants, to the prejudice of the precautions (which they deemed much more important) of simple hygiène. This had certainly been the furthest possible from the intention of those who had given the affirmative vote. A resolution, therefore, which should remove all ambiguity on this point was proposed, and unanimously adopted, as follows (I give the exact words of the resolution itself): "La science ne connait pas encore de moyens désin-
" fectants certains et spécifiques; en conséquence, la Conférence
" reconnaît une grande valeur aux mésures hygiéniques, telles que:
" aëration, lotions profondes, nettoyage, &c., combinées avec l'emploi
" des substances regardées actuellement comme désinfectantes."

No attempt was made at the present stage of proceedings to specify the various means of disinfection (as required by the last clause of the 11th question), the subject being held to belong in its details more properly to question 22 of the programme.†

Four sittings of the Conference had been occupied with the determination of these preliminary questions. The conclusions arrived at were, it will have been seen, essentially of accord with those arrived at by the Conference of Constantinople. At the last of these sittings the course to be adopted in considering the second part of the programme, the practical questions relating to Quarantine, was also discussed. It was determined that the questions relative to Land and River quarantines (questions 12–15) should be entertained in full Conference, but that the subject of Maritime Quarantine (questions 16–22) should, in the first instance, be referred to a committee, and discussed on the committee's report. It was further resolved that the questions relating to the establishment of an international sanitary commission (Part III. of Programme) should also, in the first instance, be referred to a committee. And the committees for the respective purposes were nominated.‡

II.—Questions of Quarantine.

The mode in which the questions connected with Quarantine were submitted for the consideration of the Conference differed from that which had been taken with regard to the scientific questions. The

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* In the Procès-verbaux the votes are recorded as 13 affirmative to 5 negative; M. Schleisner's vote, which was affirmative, having been erroneously entered as negative.

† In point of fact no enumeration of disinfectant substances, or recommendation as to special means of disinfection, was ever made by the Conference. The committee on Maritime Quarantines (see postea) in the Réglement attached to their report, suggested certain means as applicable to ships, and to passengers by ship, their clothes, and effects, but on discussion it was felt that the best course was to leave the choice of means of disinfection to the competent authority of each country.

‡ The committee on Maritime Quarantines, as first nominated, consisted of Messrs. Hirsch (Germany), d'Alber-Glanstätten (Austria), De Ring (France), Polak (Persia), and Seaton (Great Britain); but MM. De Ring and Polak declining, for reasons stated by them respectively, were replaced by MM. Semmola (Italy), and Van Cappelle (Holland). The committee on the subject of an International Commission consisted of MM. Lenz (Russia), Catinelli (Hungary), Marcovitz (Roumania), Kierulf (Norway), and Polak (Persia).

Conference of Constantinople, having established facts which fairly lead to the inference that a theoretically perfect Quarantine is capable of arresting cholera, had conceived and adopted a scheme for applying Quarantine, which would keep cholera, as it was supposed, eventually out of Europe. This was to be done by maritime quarantine stations on the Red and Caspian Seas and Persian Gulf, and by land quarantine stations on the Turco-Persian and Russo-Persian frontiers, and on the side of Boukhara. The scheme involved further complete temporary interruption (if necessary) of all communication between Egypt and any places in the basin of the Mediterranean. That Conference had also laid down general rules for quarantine (Régime Quarantenaire). Its scheme, as a general scheme, had never been put into execution, and indeed was in great part quite inexecutable; and it had this great defect, that it included no provision whatever for what, during the interval which had elapsed since the Conference had reported, had been the sole cause of anxiety with reference to cholera in Europe, viz., the spread of the disease in Europe itself.

The Conference of Vienna was not called upon specifically to review the several recommendations on Quarantine of the Conference of Constantinople, as it had been called on to review its conclusions on scientific matters; but certain broad general questions had been framed with the view of eliciting the opinion of the delegates assembled at Vienna as to the measures of restriction on the progress of cholera which were practicable, and likely to be efficacious, by land, by sea, or by river.

A.—*Land Quarantine.*

The 12th question on the Programme was:—"Des établissements de "quarantaine doivent-ils être construits sur terre contre le choléra?" Unless this question were answered in the affirmative, the following one, the 13th on the Programme, which had reference to the details of such establishments, fell to the ground. A resolution was proposed answering it in the negative, and adopted by a majority of 13 delegations to 4; two delegations abstaining from voting.* The terms of the resolution adopted set forth that, in view of the numerous modes of communication which existed and increased from day to day, land quarantines were inexecutable and useless; and that on this account, and on account of the serious damage they did besides to commercial interests, they ought to be abolished. (Considérant que les quarantaines de terre sont inexécutables et inutiles, vu les nombreux moyens de communication qui augmentent de jour en jour; considérant en outre qu'elles portent des atteintes graves aux intérêts commerciaux, la Conférence rejette les quarantaines de terre). Up to a certain point there was absolute unanimity of opinion in the Conference. No one contended that land quarantines on the continent of Europe, wherever a railway system had been established, were practicable; but objection was taken to the universal condemnation of land quarantines which the resolution implied. This objection was represented in three degrees (if I may so say) by three amendments successively put and negatived. The one widest from the resolution was that formulated by M. Milossavlevitch, the delegate for Servia, which, commencing by a recognition of the general utility of quaran-

* The delegations which voted against this view were those of France, Greece, Portugal, and Servia. The delegations which abstained from voting were those of Luxemburg and Switzerland. It should be stated, however, that the delegations of Turkey, Egypt, and Spain had not up to this time taken their places in the Conference.

tines, went on to say that, though land quarantines were not practicable in the centre of Europe, they ought to be established wherever topographical and social conditions admitted. This amendment received 4 votes against 13 negative; two delegations abstaining. The next, formulated by M. de Ring, delegate of France, was to the effect that the Conference was of opinion that land quarantines were in most cases impracticable, but that any States which deemed it possible to guard efficiently their land frontier by quarantines should have the liberty of doing so. This obtained 5 votes to 13 negative; one delegation only abstaining. The last amendment put, that of M. Orphanides, the delegate for Greece, proposed the maintenance of land quarantines in Greece and Turkey, on the ground that the reasons which called for the rejection of such quarantines in Europe generally did not apply to those countries. This proposal equally obtained five votes only; but of the 13 delegations which had rejected the former amendments, and which voted afterwards for the resolution originally proposed, eight abstained from voting on this amendment.* The effect was practically the same as though they had voted in the negative; an absolute majority of the delegations present being requisite for the adoption of any proposition.

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* The exceptional circumstances of Greece were ably put to the Conference by M. Orphanides; but no statement whatever of such circumstances was made on behalf of Turkey (the Turkish delegation, it should be explained, had not then arrived). On the other hand, the utter inexecutability and consequent inutility of the Turkish land quarantines were strongly stated by the Russian delegates, who, however, were amongst those who took no part in voting on this amendment. As M. Fauvel, one of the French delegation (who had not taken his place in the Conference at the time this question was discussed), has since insisted before the French Académie de Médécine on the practicability and value of these quarantines, it may not be amiss to add the following reliable description of them by Surgeon-Major W. H. Colvill, civil surgeon, Baghdad, who had himself been subjected to them:—"On my way from England last autumn, to rejoin my appointment, by "Russia and Persia, I had to spend 10 days in quarantine on the frontier at "Khanikin; and I can best give an idea of Turkish quarantine by trying to sketch "what I saw. Khanikin is a town of about 2,000 inhabitants. Here the river "Diayalah, crossed by a stone bridge, separates Turkey from Persia, and at the "Persian end, a plot of ground, bounded on one side by a canal, was marked out as "the quarantine camp, and here for two months before my arrival as many as 5,000 "travellers, Asiatic Russians, Afghans, and Persians, had at the same time been "encamped. Each company on coming in was supposed to pitch its tents a few feet "apart from the previous arrivals, though the people mixed freely together. I "arrived half an hour before midnight, and the stench from dead quadrupeds and "all manner of abominations was frightful; but that was not all, for if a person "were found dead from cholera his company had to begin the quarantine afresh, the "result being that no sooner was the breath out of the dying man than his friends "scraped a hole in the ground under the tent and pushed him in, while after them "another company would arrive, pitch on the same ground, and probably do the "same. In one case the friends were in such a hurry that they left the dead man's "beard protruding; the jackals came, and next morning his bare jawbones were "sticking through the ground. No account is kept of the arrivals, and no care "whatever is taken of the travellers, but that is no fault of the sanitary officers for "they have not the means . . . . . I was very much struck with the energy "and perseverance of the European officer here; but what could he do single-"handed amongst 5,000, constantly coming and going, men from the north, not "by any means in the best of temper, and whose language he could not under-"stand? The provisions purchased through intermediates were dear. This camp, "varying from 3,000 to 5,000, was simply a hot-bed of disease; while it did not "prevent cholera entering Turkey by that road, for it appeared at Kizil Robat, a "village of about 800 inhabitants, 16 miles on the way towards Baghdad, and for "10 days five to six people died daily; and yet this camp, behind the disease, was "kept up for a couple of months after that, while no quarantine was established "between Kizil Robat and the interior, that is towards Baghdad."— (Transactions of Medical and Physical Socioty of Bombay, N.S., No. xi. for 1871.)

The resolution, entirely condemnatory of land quarantine, was (as I have already stated) then adopted by the vote of 13 delegations to 4; two delegations abstaining.

B.—Maritime Quarantine.

It having been decided that the questions (14 and 15) which stood next in the Programme should be postponed until the subject of maritime quarantine had been discussed, the Conference next passed to that discussion, which proved an extremely animated one, and which occupied altogether nine sittings.

The discussion commenced of course with the consideration of the Report made by the Committee to whom the questions (16–22 in the Programme) relating to the subject had been referred, which Report was to the following effect:—

That maritime quarantines can only be of real use, as protective against cholera, in those ports which may be regarded as the chief points of irruption of that disease in its progress by sea towards Europe.

That, wherever instituted, they should be of the completest kind, and in conformity with the strictest rules of hygiène. That they should be international institutions.

That when cholera has broken through the chief points of irruption, quarantines in the ports of continental Europe are useless, inasmuch as the communications by land take from them all their value.

That, under these circumstances, there should be substituted in the ports of Europe for quarantine a rigorous medical inspection of every ship coming from an infected locality, in conformity with regulations which the Committee had prepared, and which it submitted to the Conference.

The general discussion of the principles involved in this Report was of the highest interest, and occupied three sittings. It was characteristic of the different stand-points from which this practical subject was approached at Constantinople and at Vienna, that, while the attention of the former Conference had, so far as it was concerned, been exclusively given to the establishment or maintenance of quarantine for the purpose of checking the progress of cholera by sea from Asia to Europe, it was with the question of the maintenance of quarantines in the ports of Europe itself that the Conference of Vienna was chiefly occupied. Little or no difference of opinion was manifested amongst those assembled at Vienna as to the utility of sea quarantines between Asia and Europe; but very great diversity of opinion was found to exist as to the advantage of such institutions in Europe itself, and it soon became evident in the progress of the debates that the Conference was divided into two camps, one comprising the majority of the delegations, who were favourable to their entire abolition in European ports, and the substitution of a system of medical inspection of vessels coming from infected places; the other, the minority, who were for maintaining them.

At the close of this general discussion, a proposal that the Report be reconsidered by the Committee with the addition of other members of the Conference entertaining views more favourable to quarantine having been rejected,* the Committee itself undertook to review its Report

* Though the Committee was unanimous in its Report, it need scarcely be said that it had not been nominated with any view to the representation in it of one set of opinions only. The Baron de Ring, the only member of the French delegation who was in Vienna when the Committee was appointed, was on the list first nominated, and on his declining to serve, a member of the Conference, whose opinions on the subject were unknown to the Conference, but generally believed to be favourable to maritime quarantine, was appointed to replace him.

before the Conference should proceed to consider and vote on the separate articles of it.

At the next sitting, (the 11th of the Conference, and 4th of the discussion on the Report,) Professor Hirsch, the reporter of the Committee, read a statement on its behalf as to the alterations and additions in the Report, which, in view of the discussion which had taken place, it deemed advisable; and the Conference then proceeded to the consideration of the Report, article by article.

The first article was as follows:—

"Les quarantaines dans les ports de mer ne peuvent offrir une protection réelle et essentielle contre le choléra que dans ces ports qui peuvent être regardés comme les points principaux d'irruption du choléra dans sa marche maritime vers l'Europe." The Committee in its supplementary statement had proposed to make this more precise by additions which should specify the Caspian and the Red Seas, with the Canal of Suez, as the chief points of the maritime irruption of cholera, and should give a positive instead of an inferential approval of quarantine being established at Astrakan and Bakou on the Caspian Sea and at El Wesch on the Red Sea.

Another "rédaction," intended, as expressly stated, to imply exactly the same thing, was moved by M. Fauvel as follows:—

"En vue de prévenir de nouvelles invasions du choléra en Europe, la Conférence approuve, en principe, les mesures recommandées par la Conférence de Constantinople, et notamment les quarantaines maritimes dans la Mer Rouge, et sur le littoral de la mer Caspienne." After some discussion a conclusion was arrived at which consisted in the adoption of the article as originally proposed by the Committee with the addition of the words, "Dans cet ordre d'idées, la Conférence adopte les conclusions de la Conférence de Constantinople, quant aux quarantaines de la Mer Caspienne et de la Mer Rouge."* It was unfortunate that in the conclusion as thus expressed the words "en principe," which were part of M. Fauvel's proposal, were omitted. For it was the general scope and intention of the proposals made on this subject by the Conference of Constantinople, and not each individual recommendation of that Conference, which was approved. The individual recommendations were in fact never discussed, and I am satisfied that I am quite correct in stating that it never entered into the mind of any delegate present at the Conference at Vienna to revive, *e.g.*, the proposal made at Constantinople for international quarantine at the straits of Bab-el-Mandeb.

Of the second article of the Committee's Report, "Ces quarantaines devraient être instituées et organisées d'une manière complète et satisfaisante selon les maximes d'hygiène les plus rigoureuses. Elles devraient être des institutions internationales," the first part was unanimously adopted. The remainder relating to the internationality of these institutions was, after a short discussion, withdrawn.

To the third article of the Report, "Contre le choléra qui a franchi les points principaux de son irruption, les quarantaines dans les ports de l'Europe continentale sont inutiles, vu que les communications par

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* A continuation, as follows, of the additional proposal of the Committee, "Quant aux ports Ottomans de la Mer-Noire, vu la position géographique de la Turquie et ses relations spéciales avec les points principaux d'irruption du choléra, cette Puissance a la liberté d'établir des quarantaines. Les Dardanelles restent dans tous les cas ouvertes au commerce international," was, at the request of the Turkish delegation, withdrawn.

" terre leur ôtent toute valeur," an amendment was proposed by M. Fauvel as follows: " Quand le choléra règne en Europe, les quarantaines " maritimes perdent en général beaucoup de leur efficacité à raison des " communications par terre. Cependant on ne saurait dire qu'elles " soient devenues entièrement inutiles." It was on these respective proposals that what I may venture to call the critical vote of the Conference took place; the result being that the resolution contained in the Committee's report for the abolition of quarantine in continental Europe, when cholera was already in Europe, was adopted by the votes of 12 delegations to 8.*

The fourth article of the report, " Dans ces conditions, il convient " d'établir dans les ports de l'Europe, au lieu des quarantaines, une inspec- " tion sanitaire rigoureuse pour chaque navire provenant d'une localité " infectée selon le règlement ci-après," was also adopted; subject, of course, to the consideration of the details of the " Règlement." These underwent much discussion, in which they were considerably improved in form, but quite untouched in principle.† As finally agreed upon they will be found inserted *in extenso* in the Annex No. III. to this abstract. In principle, the provisions are the following:—

1. Local sanitary authorities in every port for the execution of these rules; such authorities to be kept always officially informed respecting cholera in other ports.

2. Immediate free pratique to all vessels arriving from non-infected ports, which vessels, on the oath of the captain, had not during their voyage touched at any intermediate suspected port, nor communicated directly with any infected ship, and on board which there had not been any suspected or confirmed case of cholera.

3. Medical inspection, as soon as possible after arrival, of all ships coming from suspected or infected ports, as well as of ships coming from non-suspected ports, but which had during the voyage touched at any suspected port or had direct communication with any infected ship, or on which there had been any suspicious case of cholera sickness or death.

4. Immediate free pratique to the ship and everything in it, when it appeared from this inspection that there was no actual cholera, or suspected cholera, on board; except when there *had been* any such cases during the voyage, under which circumstances the ship itself, the crew and passengers, their clothes, and goods were to undergo disinfection before being admitted to pratique.

5. If on the inspection there were found any case on board of cholera or suspected cholera, or any corpse of a person suspected to have died of cholera, (1) immediate removal of the sick (if any) to hospital, and immediate burial of corpses (if any) either in the sea with usual precau-

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* Of States of the first rank, France alone voted in the minority. The delegations of Great Britain, Germany, Russia, Austria, Hungary, and Italy were ranged on the side of the majority. Again, while the 12 States constituting the majority, and comprising (in addition to the six just enumerated) Belgium, Holland, Denmark, Sweden, Norway, and Persia, were all of them maritime States, three out of the eight States constituting the minority had no maritime relations whatever, viz., Luxemburg, Switzerland, and Servia. The remaining five States in the minority were France, Portugal, Greece, Turkey, and Egypt. It should be stated, however, that the Spanish delegation, which would have undoubtedly voted with the minority, had not arrived when this vote was taken.

† More than one attempt made by M. Fauvel to break in upon the principle of the system proposed met with discomfiture. On the other hand, his criticism was of great value in making more clear and concise the provisions of the Réglement as proposed by the Committee.

tions, or on land after disinfection; (2) disinfection of the crew and passengers who were well, and of their clothes and goods; and, (3) disinfection of the ship itself. All who were well to have free pratique, with their clothes and goods, as soon as the disinfection had been accomplished.

6. Free pratique to all merchandise, except to rags and other objects of a susceptible kind which must first undergo a radical disinfection.

This system, it will be seen, is identical in principle with that which has for some time been in practice in the United Kingdom; but I had notified to the Committee at an early stage that certain of the details proposed to be introduced into the "Règlement," as, *e.g.*, the *personal* disinfection of passengers on an infected ship who were themselves certified on arrival to be unaffected with cholera or diarrhœa, with some other provisions in regard to disinfection, were not carried out, and could not be carried out, in this country in the precise way the "Règlement" directed, and that with regard to these provisions, none of which appeared to me to be fundamental, reserve would have to be made in accepting the Règlement in question.*

In the discussion which had thus far taken place on the subject of maritime quarantine, two things had become evident: (1) that whatever might be the recommendation of the Conference in regard to the substitution of a system of medical inspection for one of quarantine in Europe, there were at least some maritime States which at present would not fall in with the recommendation, and that therefore "la parfaite conformité dans les dispositions à prendre &c.," which it was the desire of those who had convoked the Conference to establish, could not as yet be arrived at; and (2) that the views of at least some of the advocates of quarantine as applied to European ports had undergone modification tending to improvement in the practice, and that probably the most important and influential of all the States still supporting the quarantine system in Europe, viz., France, would be ready to discontinue at once that system, and substitute the system of medical inspection in its northern ports, though not in all its ports, and notably not in the ports in the Mediterranean. On these grounds, and with the object of arriving as far as possible at an understanding which might be the basis of such a convention as was desired, Professor Hirsch, in the name of the committee whose views had been adopted by the Conference, proposed a further committee for considering a scheme which might be accepted by those States which for the present should decline to accept the scheme which the Conference had approved. The proposal was adopted and a committee nominated for the purpose.†

The règlement quarantenaire, which the Committee prepared and which was accepted by the Conference, is given *in extenso* in Annex III. to this abstract. It modifies considerably the practice of quarantine as heretofore carried out in Europe generally.

1–4. *As to the duration of quarantine.*—In the case of ships coming from ports known to be infected, this is fixed at from one to seven days, according to circumstances, which period however may be extended to 10 days in the Eastern States of Europe, or elsewhere under exceptional

* I think it may safely be affirmed that it was rather for the sake of countries which desired to pass from the quarantine system to the inspection system, than for countries in which, as in the United Kingdom, Sweden, Norway, Denmark, &c., such system was already in force, that the particular provisions relative to personal disinfection were introduced.

† This committee consisted of Messrs. Hirsch (Germany), d'Alber-Glanstätten (Austro-Hungary), Fauvel (France), Seaton (Great Britain), and Bartoletti (Turkey).

circumstances only. If the passage have lasted at least seven days, without there having been any suspicious case on board, the detention must be for one day only (24 hours), in other cases it may be from three to seven days, according to circumstances. In these cases, if the hygienic conditions of the vessel permit, this quarantine of observation may be performed on board, and no unloading of the vessel is required. If, however, there have been during the passage, or are found on the arrival of the ship, any cases of cholera or suspected cholera, the persons who are well are to be immediately removed and isolated in a lazaret or other place provided for the purpose, and there detained for seven full days from the date of their isolation. The sick are to be disembarked and cared for in an isolated locality, which must be quite separate from that destined for the persons under observation. After these removals, the ship itself, and all susceptible goods are to be rigorously disinfected. The persons who had necessarily remained on board are then to be the subjects of seven days' isolation and observation. In the case of ships coming from ports which are merely suspected, the duration of the quarantine of observation is not to exceed five days.

5. Ships loaded with emigrants or pilgrims, or which may be judged of especial danger to the public health, may be the subject of special precautions to be determined by the sanitary authority of the port of arrival.

6. Ships arriving at ports where there exist no efficient means of carrying out the above measures of quarantine are to receive all temporary succour that may be needed, but to be directed to the nearest port at which there is a proper establishment.

7. A ship starting from an infected port, but touching at an intermediate port, and there receiving free pratique without having performed quarantine, is to be regarded as coming from an infected port.

8. In all cases of mere suspicion, measures of disinfection may be employed when the sanitary authority thinks fit, but are not to be obligatory.

9. In any port in which cholera is already epidemic, measures of quarantine are inapplicable, and measures of disinfection should alone be practised.

The Conference added the following resolution, applicable alike whether the system of medical inspection or that of quarantine were the one adopted :—

The Captain, Medical Officer, and other Officers of ships are bound to furnish the sanitary authority of the port of arrival with every information as to any appearance or suspected appearance of disease among the crew and passengers. In case of false declaration, or of wilful concealment, they are liable to the penalties imposed by the sanitary laws of the respective countries. An international understanding on this subject would be most desirable.

The Conference also decided, in answer to question 22 of the Programme, that the modes of disinfection to be employed should be left to the competent authorities of each State.

And, at the suggestion of the delegates of Turkey, it expressed formally its desire that a penal law against sanitary offences might be promulgated in the Ottoman Empire.

C.—River Quarantine.

The Conference now returned to questions 13 and 14 of the Programme, which related to river quarantines. But the principles on which these questions were to be determined had been already all but completely discussed. It was obvious, for example, that to those parts of rivers which, whether situated exactly at their mouth or not, were really seaports, as London, Liverpool, Antwerp, the measures

decided on by each country as applicable to maritime quarantine exactly applied. It was equally obvious that all reasons which had been urged against restriction of communications by land must equally apply to rivers in their inland course. The present discussion therefore was limited almost entirely to exceptional circumstances affecting one river only, the Danube. It was with reference to this river that the second paragraph of the following conclusions, which were the conclusions of the Conference on this subject, was adopted :—

" All the reasons which have been advanced to show that land quarantines are impracticable and useless in preventing the propagation of cholera are equally valid against quarantines in the course of rivers.

" Still the measures recommended in the system of medical inspection approved by the Conference may be applied to ships having cholera on board.

" Ports at the mouths of rivers enter into the category of sea ports, and are to be so dealt with."

III.—The International Sanitary Commission.

The questions 23–26 in the Programme, which related to the institution of an International Commission for the purpose of opposing the spread of epidemics (à combattre les epidémies) had, as already stated, been referred in the first instance to a Committee; and, on the Committee's Report, the subject now came before the Conference for consideration. Two sittings were devoted to the discussion, which resulted in a very general, indeed almost unanimous, accord. The conclusions arrived at are given *in extenso* in Annex III. First, there was a universal recognition of the advantages which might be derived form the establishment of an International Commission for the further investigation of cholera and other epidemic diseases; but there was also almost complete unanimity of opinion that such Commission should be of a purely scientific character, without any administrative functions whatever. Further, it was agreed that such Commission might be consulted, by any of the Governments concerned, in regard to scientific questions, but in regard to such only. Its principal subject was to be the etiology and the prophylaxy of cholera; but it was to include the study of other epidemics also, yellow fever and plague being particularly contemplated. It was proposed that the Commission should prepare a progamme of scientific observation and research into the etiology and prophylaxy of these several epidemics, which should be carried out on a uniform plan by the several States; that it should publish the results of its work; and should have the faculty of proposing the convocation of international sanitary conferences. Secondly, it was proposed that the Commission should consist of medical men, delegated by the respective Governments assenting to the proposal, and should hold its sittings from time to time; but that there should be a central bureau, appointed and composed as the Commission itself should determine, always open. The Governments participating were to see, through their several sanitary authorities, that the international commission was supplied with all information relating to the subjects it had under investigation. Thirdly, the investigations in each country were to be of course undertaken by the sanitary authorities of the respective countries; but in any countries in which there was no organised sanitary service, the investigation might be undertaken by the international commission itself, with the consent of the Government concerned, either by means of physicians resident at fixed sanitary posts, or by temporary missions of inquiry; these in any case receiving their instructions direct from, and

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rendering their account direct to, the International Commission. The Conference left the subject of providing for the expenses of the proposed commission to be settled diplomatically between the Governments concerned.

It concluded this part of its work by the expression of its earnest desire to see instituted in Persia an international Council of Health analogous to the Councils of Health which act with such advantage at Constantinople and at Alexandria.

The particular kinds of questions relative to cholera which the international commission, if appointed, might, in the first instance, advantageously take up were indicated by various delegates in the discussions, and were some of them detailed by Professor Pettenkofer in a note which will be found attached to the third part of the Relevé des Conclusions in Annex III. But this note, it must be distinctly understood, was only meant as a *specimen* of questions waiting for solution; and was not in the least intended as even a sketch of a complete plan of work for the commission to undertake. The determining the exact commencement of cholera in each locality, and the tracing exactly its progress and termination were considered among the first duties of the Commission; the regular and systematic study of the meteorological and telluric conditions of certain specified places was another; a more exact and analytical study than we have had at present of the breaking out of cholera on board ships was another; determination of the precise duration of the incubation of cholera, determination of the value of disinfectants, &c., were all among the specimen subjects.

IV.—Quarantine against other Diseases than Cholera.

A short sitting was devoted to hearing several communications on yellow fever, but it was unanimously decided that this question should be reserved for the international sanitary commission which it was proposed to institute.

(Copy.)

ANNEX I.

Letter of Count Andrássy to the Austrian Ambassador at the Court of St. James.

Monsieur le Comte, Vienne, le 3 Mai 1874.

Depuis quelque temps déjà et de plusieurs côtés le désir s'est manifesté d'examiner de nouveau la question de savoir où et sous quelles conditions prennent naissance et s'étendent certaines épidémies qui, comme le choléra Asiatique, n'ont pas cessé, pendant les dernières années, de désoler le monde par leurs ravages, et d'entraver, par leurs perturbations, le développement des relations internationales. On a appuyé à cette occasion, sur la nécessité de faire généralement appliquer les remèdes les plus aptes pour préserver les populations contre les atteintes de ce fléau, et sur l'urgence d'étudier et de faire connaître de nouvelles mesures préventives et recommandées à cet effet par l'expérience. Le besoin s'est fait sentir, en même temps, de concerter entre les États intéressés des arrangements obligatoires qui auraient pour but d'amener une parfaite conformité dans les dispositions à prendre pour se prémunir contre ce danger commun, de concentrer et de raffermir par là les moyens de se protéger contre l'invasion de ces maladies, et

d'écarter aussi bien la confusion qui a envahi, peu-à-peu, le terrain, des principles hygiéniques en vigueur par rapport à ces épidémies et aux barrières qu'on leur oppose, que de faire disparaître les causes qui ne portent que trop souvent le trouble dans les transactions commerciales.

L'augmentation continuelle des relations commerciales entre les différents pays, et la variété des moyens de communication par lesquels le commerce est entretenu, prouvent tous les jours d'avantage, l'utilité, voire même la nécessité, d'établir des règles identiques destinées à régir ces rapports, et de les sanctionner par des conventions internationales. De nombreuses expériences démontrent les avantages de pareils arrangements. Si le libre exercice de la souveraineté territoriale est limité, en quelque sorte, par les conventions de ce genre, il est incontestable que le profit que chaque état en retire, l'emporte de beaucoup sur cet inconvénient, qui n'est qu'apparent. La pratique démontre aussi les grands désavantages qui résultent, p. e., dans le domaine de l'hygiène publique, de la divergence des principes d'après lesquels on combat, dans l'un ou dans l'autre état, les épidémies générales se propageant de pays en pays sous la tutèle, pour ainsi dire, de ces principes. Cette vérité a dès 1866 été reconnu par les Gouvernements qui ont pris part à la Conférence Sanitaire Internationale réunie à Constantinople et à laquelle on avait assigné pour objet des questions semblables à celles que nous proposons de résoudre, et un but analogue à celui que nous voulons atteindre. Des hommes de la science sérieux et compétents n'ont pas hésité dans les délibérations de la dite Conférence, à proclamer les mêmes idées auxquelles nous nous sommes associés aujourd'hui. Les conclusions adoptées par cette Conférence renferment des conseils précieux qui ne sont peut-être affectés que d'un seul défaut, celui de n'avoir jamais été mis en pratique.

Il s'agit, donc, aujourd'hui, dans cet ordre d'idées, de réviser, jusqu'à un certain point au moins, les délibérations engagées et les résolutions prises à ce sujet à Constantinople, de les vérifier et de les compléter par les idées et expériences acquirés, et surtout, d'en assurer l'exécution, et d'arrêter à cet effet entre les États intéressés, une convention sanitaire internationale qui réponde à tous besoins de la situation actuelle.

Nous avons cru ne pas devoir nous montrer indifférents à ces demandes renouvelés récemment encore et avec insistance, ainsi qu'en font foi les résolutions du troisième Congrès International de Médécine réuni en l'année passée. Guidés par ces considérations, nous nous sommes adressés aux Puissances intéressés, afin d'être informés si elles sont disposées à envoyer des délégués à une conférence sanitaire internationale, convoquée à Vienne, dans le but de délibérer et de décider sur certaines questions de réforme du service sanitaire international. Nous avons eu la satisfaction de pouvoir constater que l'initiative prise par nous à cet égard a été saluée de tout côté avec un vif empressement, et que nos propositions ont été accueillies favorablement par tous les Gouvernements auxquels nous nous étions adressés. Nous avons pensé devoir, dans ces circonstances, faciliter la tâche importante dévolue à la Conférence en faisant élaborer, par une Commission spéciale, un programme de ces travaux futurs, qui traçât dès à présent, sans limiter la liberté des appréciations et l'indépendance nécessaire de ces membres, le cadre des questions à traiter, et qui indiquât le but qu'on se propose atteindre. En prenant d'avance connaisance de ce programme, on sera mis en état de pouvoir faire soigneusement étudier ces questions, et il sera possible de munir les délégués d'instructions précises et assez étendues pour procéder plus tard en pleine connaissance de cause, aux délibérations et à la conclusion des arrangements internationaux.

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Aujourd'hui ces travaux préparatoires étant terminés, et pour ne pas retarder plus longtemps la réalisation d'un projet dont le besoin se fait sentir d'une manière impérieuse, il ne nous reste qu'à inviter officiellement tous les États intéressés dans cet affaire, à envoyer leurs délégués, munis des pleins pouvoirs nécessaires, à la Conférence Sanitaire Internationale qui est convoquée à Vienne pour le 15 Juin prochaîn, et qui sera chargée de délibérer et de décider sur les questions indiquées dans le programme. Les délégués envoyés à cette Conférence seront chargés, en outre, de s'entendre sur les bases d'un arrangement à conclure à ce sujet, et d'arrêter une convention sanitaire internationale destinée a règler les relations futures des États intéressés par rapport aux différentes questions traitées dans la Conférence. La ratification de cette Conférence devrait être réservée aux Gouvernements dont les délégués interviendraient à cette Conférence, et la faculté d'y accéder plus tard, aux États qui n'auraient pas pris part aux négociations.

Nous sommes ensuite d'avis qu'il faudrait abandonner aux Gouvernements qui prennent part à la Conférence, le soin de fixer le nombre de leurs délégués, tout en maintenant le principe que les délégués de chaque État ne pourraient disposer en votant que d'une seule voix.

Je vous prie, M. le Comte, de vouloir bien adresser cette invitation officielle au Gouvernement auprès duquel vous avez l'honneur d'être accrédité, de lui exposer les vues et les intentions qui nous animent dans cette affaire, et de lui communiquer le programme ci-joint de la Conférence. Nous vous plaisons à espérer que la Gouvernement de la Grande Bretagne reconnaîtra les valeurs des considérations qui nous ont engagés à cette démarche.

Veuillez nous faire connaître aussitôt que possible, les noms des délégués qui le Gouvernement de Grande Bretagne se propose d'envoyer à la Conférence, et recevoir, M. le Comte, l'assurance de ma considération la plus distinguée.

(Signé) Andrássy.

ANNEX II.

Programme de la Conférence Sanitaire Internationale convoquée à Vienne.

Questions préalables.

Si l'on se reporte aux débats bien connus de la Conférence sanitaire internationale de Constantinople en 1866, il importe avant tout d'examiner et de résoudre les questions préalables suivantes :

1. Le choléra Asiatique susceptible de s'étendre (épidémique) ne se développe-t-il spontanément que dans l'Inde, et est-ce toujours du dehors qu'il arrive, quand il éclate dans d'autres pays ? Ou bien revêt-il aussi le caractère endémique dans d'autres pays que l'Inde ? dans ce cas quels sont ces pays ?
2. Le choléra est-il transmissible par l'homme ?
3. Le choléra peut-il être propagé par des effets, qui, provenant d'un lieu infecté, ont servi à l'usage et spécialement par ceux qui ont appartenu à des cholériques ?
4. Peut-il être propagé par des comestibles ?
5. Peut-il être importé par des animaux vivants ?
6. ou par le transport de marchandises ?
7. ou, enfin, par les cadavres des cholériques ?
8. Le choléra peut-il se propager au loin par l'atmosphère seule ?
9. L'air frais arrivant du dehors aux agents donnant naissance ou propageant le choléra, et les aërant, ou bien l'isolement de ces agents de

l'air extérieur constituent-ils des éléments ayant ou non une influence sur le caractère contagieux de choléra ?

10. Quand il y a contagion, quelle est la durée de l'incubation ?

11. Connaît-on des moyens ou des procédés de désinfection grâce auxquels le principe générateur ou contagieux du choléra peut sûrement ou avec quelque chance de succès être détruit et perdre de son intensité ?

Dans le cas affirmatif quels sont ces moyens ?

Questions sur les Mesures de Quarantaine en Temps de Choléra.

12. Des établissements de quarantaine doivent-ils être construits sur terre contre le choléra ?

13. Dans ce cas :

(*a.*) Où seront-ils placés ?

(*b.*) Quand et dans quelles conditions ces constructions doivent-elles se faire ?

(*c.*) Quelles seraient les conditions à remplir sous le rapport des bâtisses et sous celui de l'organisation administrative ?

(*d.*) Comment et par quels moyens est-il possible d'empêcher l'accès dans un pays par une autre voie que celle protégée par des établissements de quarantaine ?

14. Des établissements de quarantaine contre le choléra doivent-ils être aussi construits sur les bords des fleuves ?

15. Dans le cas affirmatif (comme au § 13) ?

16. Doit-on construire des établissements de quarantaine maritimes ? ou conserver ceux qui existent ?

17. Si tel doit être le cas (comme au § 13) ?

18. Quels sont les principes qui doivent être adoptés envers les personnes

(*a.*) pour les admettre immédiatement à la libre pratique ?

(*b.*) pour leur faire subir une quarantaine d'observation ?

(*c.*) ou une quarantaine rigoureuse ? (Établissements de quarantaine, lazaret.)

19. Quelle doit-être, pour les personnes saines (passagers, marins, etc.), la durée

(*a.*) de la quarantaine d'observation ? et,

(*b.*) de la quarantaine rigoureuse proprement dite ?

quelle est pour les personnes atteintes du choléra, la durée du séjour au lazaret ?

20. Sous quelles conditions et dans quelle mesure peut-on comprendre, pour des navires, la durée de la traversée dans le temps fixé pour la quarantaine ?

21. Quels sont les principes qui seront appliquées

(*a.*) aux effets qui servent à l'usage de personnes,

(*b.*) aux animaux vivants,

(*c.*) aux marchandises,

(*d.*) aux comestibles,

(*e.*) aux navires, wagons, voitures, etc.,

pour les admettre à la libre pratique sans qu'ils n'aient été désinfectés ou après qu'ils l'ont été ?

22. En quoi consiste la désinfection

(*a.*) des personnes,

(*b.*) des effets à leur usage,

(*c.*) des animaux vivants,

(*d.*) des marchandises,

(*e.*) des moyens de transport ? (Moyens, mode et durée de l'application.)

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Questions au sujet de l'Institution d'une Commission Internationale appelée à Combattre les Epidémies.

23. Des postes sanitaires permanents, ou temporaires et internationaux, qui auraient à s'occuper d'étudier les épidémies et de rechercher les moyens d'empêcher la propagation, doivent-ils être établis pour tous les genres d'épidémie ou seulement pour certaines catégories, et dans ce dernier cas pour quelles ?

24. Dans le cas affirmatif :

(*a.*) où ces postes sanitaires seront-ils établis ?
(*b.*) quelle organisation leur donnera-t-on ?
quel sera leur personel ?
en quoi consisteront les localités ?
les ressources scientifiques ?
quels seront les appointements ?
comment se procurera-t-on les fonds nécessaires ?
(*c.*) qui aurait à nominer le personnel ?
(*d.*) de quelle autorité relèveront ces postes ?
(*e.*) d'après quels principes et par qui leurs instructions seront-elles rédigées ?

5. Une Commission sanitaire permanente ou temporaire et internationale qui aurait à s'occuper d'étudier les épidémies et de rechercher les moyens d'empêcher leur propagation doit-elle être établie pour tous les genres d'épidémie ou seulement pour certaines catégories, et, dans ce cas, pour lesquelles cette Commission aurait-elle en même temps à décider certaines questions de quarantaine internationales dans des cas donnés et quels sont ces cas ?

26. Dans le cas affirmatif :

(*a.*) où doit être le siège de cette Commission ?
(*b.*) quelle doit en être l'organisation,
le personnel,
les établissements,
les ressources scientifiques,
les appointements,
et comment fera-t-on les fonds ?
(*c.*) qui aurait à en désigner les membres et qui à choisir le reste du personnel ?
(*d.*) quelle sera la position officielle à donner à cette Commission et quelle sera sa sphère d'action ?

Questions relatives à des Mesures de Quarantaine à prendre contre des Épidémies pouvant régner parmi les Hommes et qui sont autres que le Choléra.

Il reste réservé à la Conférence Sanitaire Internationale de faire figurer dans son programme, outre les mesures de quarantaine à prendre contre le choléra, de même aussi celles qu'elle jugera utile d'arrêter contre d'autres épidémies susceptibles de régner parmi les hommes.

ANNEX III.

Relevé des Conclusions adoptées par la Conférence Sanitaire Internationale de Vienne.

Première Partie.

Questions Scientifiques.

I.

Origine et Genèse du Choléra; Endémicité et Epidémicité de cette Maladie dans l'Inde.

Le cholera asiatique, susceptible de s'étendre (épidémique), se développe spontanément dans l'Inde, et c'est toujours du dehors qu'il arrive, quand il éclate dans d'autres pays.

Adopté à l'unanimité.

Il ne revêt pas le caractère endémique dans d'autres pays que l'Inde.

Adopté à l'unanimité.

II.

Questions de Transmissibilité.

1°. *Transmissibilité par l'Homme.*

La Conférence accepte la transmissibilité du choléra par l'homme venant d'un milieu infecté; elle ne considère l'homme comme pouvant être la cause spécifique, qu'en dehors de l'influence de la localité infectée; en outre, elle le regarde comme le propagateur du choléra, lorsqu'il vient d'un endroit où le germe de la maladie existe déjà.

Adopté à l'unanimité.

2°. *Transmissibilité par les Effets à Usage.*

Le choléra peut être transmis par les effets à usage provenant d'un lieu infecté, et spécialement par ceux qui ont servi aux cholériques; et même il resulte de certains faits, que la maladie peut être importée au loin par ces mêmes effets renfermés à l'abri du contact de l'air libre.

Adopté à l'unanimité.

3°. *Transmissibilité par les Aliments et les Boissons.*

(*a.*) *Aliments :*

La Conférence, ne possédant pas de preuves concluantes pour la transmission du choléra par les aliments, ne se croit pas autorisée à prendre une décision à cette égard.

Résultat du vote : 11 oui, 7 non.

(*b.*) *Boissons :*

Le choléra peut être propagé par les boissons, particulièrement par l'eau.

Adopté à l'unanimité.

4°. *Transmissibilité par les Animaux.*

On ne connaît aucun fait probant de la transmissibilité du choléra par les animaux à l'homme, mais il est très-rationnel d'en admettre la possibilité.

Résultat du vote : 10 oui, 2 non, 6 abstentions.

5 *De la Transmissibilité par les Marchandises.*

Tout en constatant, à l'unanimité, l'absence de preuves à l'appui de la transmission du choléra par les marchandises, la Conférence a admis la possibilité du fait dans certaines conditions.

Resultat du vote : 13 oui, 5 abstentions.

6°. *Transmissibilité par les Cadavres Cholériques.*

Bien qu'il ne soit pas prouvé par des faits concluants que les cadavres de cholériques puissent transmettre le choléra, il est prudent de les considérer comme dangereux.

Adopté à l'unanimité.

7°. *Transmissibilité par l'Atmosphère seule.*

Aucun fait n'est venu prouver jusqu'ici que le choléra puisse se propager au loin par l'atmosphère seule, dans quelque condition qu'elle soit ; en outre, c'est une loi, sans exception, que jamais une épidémie de choléra ne s'est progagée d'un point à un autre dans un temps plus court que celui nécessaire à l'homme pour s'y transporter.

L'air ambiant est le véhicule principal de l'agent générateur du choléra ; mais la transmission de la maladie par l'atmosphère reste, dans l'immense majorité des cas, limitée à une distance très-rapprochée du foyer d'émission. Quant aux faites cités de transport par l'atmosphère à un ou plusieurs milles de distance, ils ne sont pas suffisamment concluants.

Adopté à l'unanimité.

8°. *Action de l'Air sur la Transmissibilité.*

Il résulte de l'étude des faits qu'à l'air libre le principe générateur du choléra perd rapidement son activité morbifique, telle est la règle ; mais dans certaines conditions particulières de confinement, cette activité peut se conserver pendant un temps indéterminé.

Le choléra peut être transmis par les effets à usage provenant d'un lieu infecté, et spécialement par ceux qui ont servi aux cholériques ; et même il résulte de certains faits que la maladie peut être importée au loin par ces mêmes effets renfermés à l'abri du contact de l'air libre.

Les grands déserts sont une barrière très-efficace contre la propagation du choléra, et il est sans exemple que cette maladie ait été importée en Egypte ou en Syrie, à travers le désert, par les caravanes parties de la Mecque.

Adopté à l'unanimité.

III.

Durée de l'Incubation.

Dans presque tous les cas, la période d'incubation, c'est à dire le temps écoulé entre le moment où un individu a pu contracter l'intoxication cholérique et le début de la diarrhée prémonitoire ou du choléra confirmé, ne dépasse pas quelques jours. Tous les faits cités d'une incubation plus longue se rapportent à des cas qui ne sont pas concluants, ou bien parce que la diarrhée prémonitoire a été comprise dans la période d'incubation, ou bien parce que la contamination a pu avoir lieu après le départ du lieu infecté.

L'observation montre que la durée de la diarrhée cholérique, dite prémonitoire—qu'il ne faut pas confondre avec toutes les diarrhées qui existent en temps de choléra—ne dépasse pas quelques jours.

Les faits cités comme exceptionnels ne prouvent pas que les cas de diarrhée qui se prolongent au-delà appartiennent au choléra, et soient susceptibles de transmettre la maladie, quand l'individu atteint a été soustrait à toute cause de contamination.

Résultat du vote : 13 oui, 1 non, 4 abstentions.

IV.

Questions de la Désinfection.

1°. Connaît-on des moyens ou des procédés de désinfection, grâce auxquels le principe générateur ou contagieux du choléra peut sûrement être détruit ou perdre de son intensité ?

Résultat du vote : 12 non, 7 abstentions.

2°. Connaît-on des moyens ou des procédés de désinfection, grâce auxquels le principe générateur ou contagieux du choléra peut avec quelque chance de succès être détruit ou perdre de son intensité ?

Resultat : 13 oui, 5 non.

3°. La science ne connaît pas encore de moyens désinfectants certains et spécifiques : en conséquence, la Conférence reconnaît une grande valeur aux mesures hygiéniques telles que : aëration, lotions profondes, nettoyage, etc., combinées avec l'emploi des substances regardés actuellement comme désinfectants.

Adopté à l'unanimité.

DEUXIÈME PARTIE.

Questions des Quarantaines.

I.

Quarantaines de Terre.

Considérant que les quarantaines de terre sont inexécutables et inutiles, vu les nombreux moyens de communication qui augmentent de jour en jour ; considérant en outre qu'elles portent des atteintes graves aux intérêts commerciaux, la Conférence rejette les quarantaines de terre.

Résultat du vote : 13 oui, 4 non, 2 abstentions.

II.

Quarantaines Maritimes.

I.

Mesures à prendre en dehors de l'Europe

En vu de prévenir de nouvelles invasions du choléra en Europe, la Conférence approuve les mesures recommandées par la Conférence de Constantinople, notamment les quarantaines dans la Mer-Rouge et dans la Mer-Caspienne.

Ces quarantaines devront être instituées et organisées d'une manière complète et satisfaisante, selon les maximes d'hygiène les plus rigoureuses.

II.

Mesures à prendre dans les Ports de l'Europe.

Lorsque le choléra a fait invasion en Europe, la Conférence recommande le système d'inspection médicale, mais pour les États que préfèrent maintenir les quarantaines, elle établit les bases d'un règlement quarantenaire.

A. *Système de l'Inspection médical.*

1. Il y aura, dans chaque port ouvert au commerce, une autorité sanitaire composée de médecins et d'administrateurs, aidés par un personnel de service. Le nombre des membres de ces différentes catégories variera dans chaque port selon l'importance du mouvement maritime, mais il devra être suffisant pour pouvoir accomplir dans toutes les circonstances et avec rapidité les mesures exigées pour les navires, les équipages, et les passagers.

Le chef de ce service sera toujours tenu au courant par des communications officielles de l'état sanitaire de tous les ports infectés de choléra.

2. Les navires provenant d'un port net, n'ayant (d'après la déclaration, sous serment, du capitaine) touché dans leur voyage aucun port intermédiaire suspect, ni communiqué directement avec aucun navire suspect, et sur lesquels durant le voyage on n'aura constaté aucun cas suspect ou confirmé de choléra, auront la libre pratique.

3. Les navires provenant d'un port suspect ou infecté et ceux provenant de ports non suspects, mais qui ont eu dans le voyage des rélations intermédiaires compromettantes, ou sur lesquels il y a eu durant la traversée des cas suspects de maladie ou de mort de choléra, seront soumis dès leur arrivée à une visite médicale rigoureuse pour constater l'état sanitaire du bord.

4. S'il résulte de la visite médicale qu'il n'existe parmi les hommes de l'equipage et les passagers aucun cas suspect de maladie ou de mort de choléra, le navire, avec tout ce qu'il renferme, sera admis à la libre pratique. Mais si des cas de choléra ou de nature suspecte se sont manifestés à bord durant la traversée, le navire, les vêtements et les effets à usage des gens de l'équipage et des passagers seront soumis d'abord à une désinfection rigoureuse, bien que l'équipage et les passagers aient été trouvés indemnés du choléra dans le port.

5. S'il y a à l'arrivée des cas suspects de maladie ou de mort de choléra, les malades seront immédiatement transportés dans un lazaret ou dans un local isolé pouvant en tenir lieu et prêt à les recevoir; les cadavres seront jetés à la mer avec les précautions d'usage ou ensevelis après avoir été convenablement désinfectés; les passagers et l'equipage seront soumis à une désinfection rigoureuse, et le navire lui-même sera désinfecté, après qu'on en aura éloigné les passagers et la partie du personnel de l'équipage qui n'est pas nécessaire à la désinfection et à la surveillance.

Les vêtements et les effets à usage des malades et même des passagers sains seront assujettis, dans un local spécial et sous le contrôle rigoureux de l'autorité sanitaire, à une radicale désinfection.

Après cette désinfection, les effets seront rendus aux passagers et aux personnes de l'équipage qui seront admis à libre pratique.

6. Les marchandises débarquées seront admises à libre pratique, à l'exception des chiffons et autres objets susceptibles, que l'on devra soumettre à une radicale désinfection.

B. Système des Quarantaines.

Provenances de Ports Infectés.

1°. Les provenances de ports infectés sont soumises à une observation variant de 1 à 7 jours pleins selon les cas. Dans les ports des États orientaux de l'Europe, et ailleurs dans certains cas exceptionnels seulement, la durée de l'observation peut être portée à 10 jours.

Navires suspects.

2°. Si l'autorité sanitaire a la preuve suffisante qu'aucun cas de choléra ou de nature suspecte n'a eu lieu à bord durant la traversée, la durée de l'observation est de 3 à 7 jours, à dater de l'inspection médicale.

Si dans ces conditions la traversée a duré au moins 7 jours, l'observation est réduite à 24 heures pour les constatations et les désinfections qui pourraient être jugées nécessaires.

Dans les cas de cette catégorie, la quarantaine d'observation peut être purgée à bord, tant qu'aucun cas de choléra ou d'accidents suspects ne s'est manifesté, et si les conditions hygiéniques du navire le permettent.

Dans ces cas le déchargement du navire n'est point obligatoire.

Navires infectés.

3°. En cas de choléra ou d'accidents suspects soit durant la traversée, soit après l'arrivée, la durée de l'observation pour les personnes non malades est de 7 jours pleins, à dater de leur isolement dans un lazaret ou dans un endroit pouvant en tenir lieu.

Les malades sont débarqués et reçoivent les soins convenables dans un local isolé et séparé des personnes en observation.

Le navire et tous les objets susceptibles sont soumis à une désinfection rigoureuse, après laquelle les personnes restées à bord du navire sont assujetties à une observation de 7 jours.

Provenances de Ports suspects.

4°. Les provenances des ports suspects, c'est-à-dire voisins d'un port où règne le choléra et ayant des relations libre avec ce port, peuvent être soumises à une observation, qui n'excédera pas 5 jours, si aucun accident suspect ne s'est produit à bord.

Dispositions diverses.

5°. Les navires chargés d'émigrants, de pélerins, et, en général, tous les navires jugés particulièrement dangereux pour la santé publique, peuvent, dans les conditions mentionnées précédemment, être l'objet de précautions spéciales que déterminera l'autorité sanitaire du port d'arrivée.

6°. Lorsque les ressources locales ne permettent pas d'exécuter les mesures ci-dessus prescrites, le navire infecté est dirigé sur le plus prochain lazaret, après avoir reçu tous les secours que réclame sa position.

7°. Un navire provenant d'un port infecté, qui a fait escale dans un port intermédiaire et y a reçu libre pratique sans avoir fait de quarantaine, est considéré et traité comme provenant d'un port infecté.

8°. Dans les cas de simple suspicion, les mesures de désinfection ne sont pas de rigueur, mais elles peuvent être pratiquées toutes les fois que l'autorité sanitaire le juga convenable.

9°. Un port où le choléra règne épidémiquement ne doit plus appliquer de quarantaine proprement dite, mais doit pratiquer seulement des mesures de désinfection.

C.—Dispositions Communes aux Deux Systèmes.

(*Inspection médicale.—Quarantaines.*)

1. Le capitaine, le médécin, et les officiers du bord sont tenus de déclarer à l'autorité sanitaire tout ce qu'ils peuvent savoir d'apparition suspecte de maladie parmi l'équipage et les passagers.

En cas de fausse déclaration ou de réticence calculée ils sont passibles des peines édictées par les lois sanitaires. Il serait à désirer qu'une entente internationale s'établit à ce sujet.

2. La désinfection soit des effets à usage, soit des navires, sera opérée par les procédés que les autorités compétentes de chaque pays jugeront les mieux appropriés aux circonstances.

La Conférence adopte : 21 oui, 1 abstention.

La Conférence exprime le vœu qu'une loi pénale applicable aux contraventions sanitaires soit édictée dans l'Empire Ottoman.

Fesultat du vote : 15 oui, 4 non, 3 abstentions.

III.

Quarantaines Fluviales.

Routes les raisons produites, pour démontrer que les quarantaines par terre sont impracticables et inutiles pour empêcher la propagation du choléra, sont également valables pour les quarantaines dans le cours des fleuves.

Toutefois les mesures recommandées dans le systême de l'inspection médicale adopté par la Conférence peuvent y être appliquées aux navires ayant le choléra à bord.

Quant aux ports de l'embouchure, its rentrent dans la catégorie des ports maritimes, et par conséquent les mêmes mesures y sont applicables.

Resultat du vote : 19 oui, 3 abstentions.

TROISIÈME PARTIE.

Projet de Création d'une Commission Internationale Permanente des Epidémies.

I.

(*But.—Utilité.*)

Il sera institué à Vienne une Commission Sanitaire Internationale Permanente, ayant pour objet l'étude des maladies épidémiques.

II.

(*Attributions.*)

Les attributions de cette Commission seront purement scientifiques ; elle pourra être consultée dans les questions scientifiques.

La Commission aura pour tâche principal l'étude du choléra, au point de vue de l'étiologie et de la prophylaxie.

Néanmoins elle pourra comprendre dans ses études les autres maladies épidémiques.

A cet effet, elle tracera un programme comprenant les recherches devant être entreprises d'une manière uniforme par tous les États contractants, sur l'étiologie et la prophylaxie du choléra et des autres maladies épidémiques.*

Elle fera connaître le résultat de ses travaux.

Enfin elle pourra proposer la convocation de conférences sanitaires internationales, et elle sera chargée d'élaborer le programme de ces conférences.

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* Voir quelques exemples à l'Annexe.

III.

(*Composition.—Fonctionnement.*)

La commission sera composée de médecins délégués par les Gouvernements participants. Il y aura au siége de la Commission un bureau à résidence fixé, chargé de centraliser les travaux et de donner suite aux délibérations de la Commission générale. La nomination et la composition de ce bureau sont laissées aux soins de la Commission générale. Les Gouvernements des États participants donneront à leurs autorités sanitaires et à leurs conseils d'hygiène publique les instructions nécessaires pour fournir à la Commission internationale tous les renseignements rélatifs aux questions qui rentrent dans le cercle de ses études.

Dans les pays où des conseils sanitaires internationaux sont établis, ceux-ci fourniront tous les renseignements qu'ils possèdent, et prescriront les recherches nécessaires.

IV.

(*Voies et Moyens.*)

Les frais nécessités pour le fonctionnement de la Commission internationale seront répartis entre les divers États intéressés, et seront réglés par voie diplomatique.

V.

(*Postes et Missions.*)

Dans les pays où il n'y a pas de service sanitaire organisé, les études seront faites, avec l'assentiment du Gouvernement local, par les missions temporaires on par des médicins en résidence fixe.

Ces missions et ces postes sanitaires fixes, institués par voie internationale, seront créés d'après les indications de la Commission internationale, recevront d'elle leurs instructions, et lui rendront compte de leurs travaux.

(*Article Additionel.*)

Il serait à désirer qu'un conseil de santé international, analogue à ceux qui fonctionnent avec tant d'avantage à Constantinople et à Alexandrie, fût institué en Perse.

Un tel conseil contribuerait beaucoup par l'autorité de ses avis, donnés en connaissance de cause, à améliorer les conditions sanitaires de ce pays, et serait en même temps un puissant moyen de protection contre l'invasion des épidémies en Europe.

Annexe à l'Article II. du Projet de Création d'une Commission Internationale des Épidémies.

Comme premières recherches, la Commission pourrait s'occuper des questions suivantes :—

1°. L'étude régulière et suivie de la quantité de pluie et de la quantité d'eau d'évaporations pendant l'année dans les stations suivantes :—

Bender Bouschir,	Alexandrie,
Ispahan,	Astrakan,
Téhéran,	Bakou,
Tauris,	Tiflis.*
Suez,	

* Voir la proposition de Monsieur de Pettenkofer.

2°. L'étude scientifique des conditions telluriques de ces différentes villes.

3°. L'examen plus exact, et entrepris avec plus d'esprit d'analyse qu'il ne l'a été jusqu'ici de l'apparition et de la propagation du choléra sur les vaisseaux.

Les recherches porteront provisoirement sur quelques lignes très-fréquentées* :—

Calcutta—Maurice.
Alexandrie—Malte.
Alexandrie—Marseille.
Southampton—Amérique du Nord.
Hambourg—New York.
Singapoor—Aden—Djeddah.
Calcutta—Aden—Djeddah.
Bombay—Aden—Djeddah.
Naples—Vénise.

4°. Faire constater les premiers cas de chaque épidémie de choléra qui éclate dans les différentes localités et spécialement dans les ports maritimes de l'Europe, et réunir tous les éléments d'une statistique complète relative à la marche du choléra en Europe.

5°. Déterminer par des faits scientifiques la durée précise de l'incubation du choléra.

Adopté à l'unanimité.

QUATRIÈME PARTIE.

La Conférence a entendu plusieurs communications sur la fièvre jaune, mais elle a décidé, à l'unanimité, que cette question devait être renvoyée à la Commission internationale permanente des épidémies dont elle a proposé la création.

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* Voir Pettenkofer.

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PUBLIC HEALTH.

REPORTS

OF

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NEW SERIES, No. VI.

REPORT TO THE LORDS OF THE COUNCIL ON SCIENTIFIC INVESTIGATIONS, MADE, UNDER THEIR DIRECTION, IN AID OF PATHOLOGY AND MEDICINE.

Presented to both Houses of Parliament by Command of Her Majesty.

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To the Lords of Her Majesty's most Honorable Privy Council.

My Lords,

In further report on the Scientific Investigations which I have the honour of superintending under your Lordships, I now beg leave to submit the annexed six papers, referring to the various sections of work which were in hand during last financial year.

The *first* of them relates to the pathology of that complex bodily disturbance which is known as the *Process of Fever*.

This process, as regards the width and depth of its practical interest to persons concerned in the treatment of disease, is certainly second to none which the body suffers; for at every turn of medical practice it is apt to present itself for treatment as a more or less prominent part of the patient's total illness, and in a large proportion of such cases is an influence which involves the issues of life or death. In order that the medical treatment of the febrile process should be perfect, the process ought to be thoroughly understood in respect of all the dynamics of its constitution: so thoroughly, indeed, that the bedside practitioner shall be able to apply his counter-agents with the precision of one who conducts a merely physical experiment. Till within very recent times, however, not even the necessity for that degree of insight into the febrile process has been distinctly felt; and though in these latest times the process has been studied in such spirit of exact science as must surely sooner or later eventuate in improvements of practical efficiency, the modern studies, so far as their results have been made known, can hitherto hardly claim to have done more than contribute some preparatory elements towards the complete doctrine of the future.

Professor Sanderson, under your Lordships' commission, has during the past three years been spending much time in the investigation of this great section of pathology, and has been gradually making his knowledge of it fuller and more exact. It is scarcely needful to observe that no present treatment of the subject can be regarded as exhaustive and final; but in the annexed paper Dr. Sanderson gives, as instalment, a very elaborate critical exposition of those parts of the subject which he thinks may now be taken as settled.

The *second* paper, which is also by Dr. Sanderson, relates to the study of *Inflammation* in that extremely important point of view which regards it as an infective process.

Facts which more or less pointedly tend to establish the infectivity of the process of inflammation are familiar in the practice of surgery, and have for many years past been grouped together in

that ætiological connexion :* but, with clinical observation alone, the case could not be fully understood ; and it was indispensable for the growth of surgery in this direction that the inflammatory process, in its zymotic relations, should be carefully investigated by experiment. The studies which in the years 1867–8 and 1871–2 were made under your Lordships, with regard to the processes of tubercular infection, necessarily had regard to the infective influence of various acute inflammations ; and much new knowledge which accrued from them in this respect was embodied by Dr. Sanderson in a special report, completed in the summer of 1872.† Dr. Sanderson has recently made further investigation in the same study, and now reports again on an important section of it ; and the annexed paper, which contains his report of the present year, contains also, as requiring to be read with it, and as not before officially published, the earlier report which he presented.

The prolonged research which is represented in the two parts of the annexed paper has been of extreme pathological and practical interest : partly as an essential contribution to the general study of processes of contagion, but even more as tending to throw new light on those terrible misadventures which arise in surgical and obstetrical practice when infective inflammations develop the malignant forms of traumatic and puerperal fever.

With regard to those disastrous infections, the earlier report gives results which I have already had occasion elsewhere to quote :‡ broadly to the effect, that apparently those "pyæmic" and "septicæmic" diseases have their common essential cause in one morbid poison or contagium, which, so far as can yet be discerned, is a particulate ferment of ordinary putrefaction,§ and which, while able to produce those diseases by its intenser action, is also able (as had previously been shown) to produce by less intense action the chronic tubercular infection of the body ; and that, in animals, suffering under the acute infection, microzymes, in active process of multiplication, had uniformly been found in the exudation-liquids of the inflamed parts. Dr. Sanderson, however, had also found that inflammations, in order to be most formidably infective, need not have been started by contagion from any pre-existing case of like sort, nor by any immediate inoculation with

* Thus, in 1860, in the article "Inflammation," in Holmes's "System of Surgery," it was argued that the evidences then known were enough to prove the essential contagiousness of the process, and the general conclusion was stated as follows : "Inflammatory excitement tends to diffuse itself. Within limits hitherto not defined, inflammations, both common and specific, are communicable from part to part, and from person to person. 'Sympathetic inflammations' are facts of inflammatory contagion. 'Inflammatory fever' is a total bodily infection, wrought by materials from the inflamed part."—Op. cit., first edition, Vol. I., p. 92.

† At that time (in consequence of departmental changes) the continuity of my annual reports to my Lords of the Council had been interrupted ; and therefore, in order not to delay scientific publication of Dr. Sanderson's results, a copy of this paper was, by permission, communicated to the Royal Medical and Chirurgical society, who printed it in the next (56th) Volume of their Transactions.

‡ In Nos. II. and III. of the present series of Reports.

§ I have no intention of implying that ordinary putrefactive changes have only one ferment which can be considered habitual to them.

foreign putrid matter, but might, it seemed, be highly infective merely in accompaniment of being highly intense. And it is at about this part of the subject that the special interest of Dr. Sanderson's later report begins. For, in regard of that compound quality of infectiveness and intensity in inflammation, Dr. Sanderson has now succeeded in clearly showing that it is a quality which may be artificially cultivated; and that, starting from some purely chemical lesion, it can be developed in higher and higher degrees by successive inoculations from subject to subject, till there presently results one of the most tremendous morbid poisons which the mind of the pathologist can conceive.

The *third* paper, which is by Dr. Klein, gives (as foreshadowed in my last report) the extremely interesting results of his investigation of the intimate anatomy of *Enteric Fever;* and Dr. Klein, who fortunately is artist enough to reproduce admirably with his pencil the anatomical appearances which he displays under the microscope, has here, as on former occasions, illustrated his written report with drawings which make the results peculiarly clear.

The paper has its distinctive and very great interest in the fact that it purports to describe for the first time the contagium of enteric fever as something cognizable to the eye: in respect of certain multiplying microscopical forms, apparently of the lowest vegetable life, which are found in innumerable swarms in the bowel-textures and bowel-discharges of the sick; penetrating from the former to diffuse throughout the patient's general system, and teeming in the latter to represent, as this view supposes, the possible germs of epidemic infection.

The most cursory glance cast by the anatomist at the illustrations of Dr. Klein's paper will convince him of the reality of the facts which Dr. Klein interprets to the above effect: and, that the interpretation thus assigned to the facts is the one which they must generally receive is, I think, an inevitable consequence of considerations which were stated in my last report with general regard to agencies of contagion. The enteric fever of man is not yet known to be communicable to any other animal; and it has therefore not been possible to perform in relation to its supposed contagium such experiments as have been made on the lower animals with respect to the contagia of some other diseases. In absence of such experiments, the same degree of certainty cannot at present be expressed with regard to the contagium of enteric fever as with regard to that (for instance) of sheep-pox: but, subject to any correction which experiment may hereafter supply, we may at least accept as approximately proven, that the contagium of enteric fever has its essence, or part of its essence, in the microphyte which Dr. Klein has discovered; and that here accordingly is a further illustration of the general doctrine which I have noticed on many previous occasions, with regard to the significance of specific organic forms in the constitution of specific contagia.

In an immediately practical point of view, much interest

attaches to Dr. Klein's remark that the microphyte which he describes in the present paper closely corresponds with that which Professor Cohn, the eminent micro-botanist, described, under the name of Crenothrix polyspora, as found by him "in the well-water of a certain district in Breslau, famous for the frequent occurrence of enteric fever among its inhabitants."

The *fourth* paper, which is by Dr. Creighton, reports the continuation of the research in which he has been engaged, in introduction to the ætiology of *Cancer*.

In agreement with general principles which modern pathology illustrates more and more strongly in proportion as its own progress advances, and the importance of which is asserting itself to the utmost in the present matter, it had appeared that, before there could be any reasonable hope of understanding for preventive purposes the dynamics of the production of cancer, there was need, in the first place, that the process of the disease should admit of being identified in the earliest movement of its divergence from health; and therefore that, in regard of any organ in which the disease had to be investigated, the observer should know with absolute accuracy the normal texture-changes of the organ.

Dr. Creighton has for the past two years been working in that sense at the genesiology of cancer: working, namely, from the point of view which regards, as first matter for interpretation, the finer anatomy of the disease. His report of last year gave the results of a very careful study of the beginnings of cancer in organs secondarily affected by it, as specially in the liver; and in that report he not only expressed very definite conclusions as to the mode of origin of the secondary tumours—both as to the anatomical elements in which they begin and as to the physiological analogies of their beginning, but intimated also that the observations which he had made in that respect were in his opinion highly suggestive with regard to the probable mode of origin of the primary disease. In the report of the present year, account is given of a very thorough following of that line of suggestion so far as relates to one organ of the body; namely, *the Breast;* an organ, the interest of which in the present context may be ranked as of the highest order. In the first part of the paper, Dr. Creighton reports the results of his investigation (far more exact than had ever previously been made) with regard to the development of the mammary gland, and to the processes of change which the adult female breast normally undergoes in its alternations of activity and rest, and to the relations of the lymphatic system to these changes; and in the second part of the paper he exhibits the development and infectiveness of primary cancerous tumours of the breast as standing in the clearest connexion with the morphological history which he has premised.

The *fifth* paper relates to that branch of the Investigations which is in the hands of Dr. Thudichum, and which consists distinctively in the chemical division of our subject-matter.

Dr. Thudichum during the past year has been very actively continuing the great research on which he reported a year ago in introduction to the *Chemical Pathology of the Nervous System*; but, as regards this further work, he is not yet prepared to do more than report provisionally some of the more interesting separate results which have been obtained. Of these the chief refers to the existence of Alkaloids in the Brain, and specially of one alkaloid which has properties of a new type. Incidentally to the investigation of the brain-alkaloids, Dr. Thudichum had to acquire more exact knowledge as to the distribution of alkaloids elsewhere in the animal body; and in his annexed paper he briefly records the results which he thus got in relation to muscular tissue, and to milk and albumen and urine.

The *sixth and last* paper of the annexed series is by Dr. Baxter, who reports in it the results of an experimental study which he has made of the amenability of certain contagia to control by certain officinal *Disinfectants.*

Last year, when I was reporting to the Local Government Board, on some of the chief infections which prevail in this country,* practical considerations obliged me to point out in regard of them (and the same observation applies generally to infectious disease) that much procedure which popularly passes among us under the name of "disinfection," is but the most futile of ceremonies; and in contrast with such, I referred to the very real services which might fairly be expected from Chemistry, if skilfully used within its appropriate sphere of operation. It is in relation to individual cases of infectious disease, and in endeavours to secure in detail (so far as possible) the immediate neutralisation of the infectious matters which come from the sick, that Chemistry has its chief opportunities of subserving preventive medicine; but in any such endeavours for disinfection, everything must turn on the accuracy and completeness with which each prescribed performance is done; and it is evident that prescriptions for disinfection ought to have the same sort of exactness as prescriptions which are for therapeutical purposes. Exactness such as this is only possible in proportion as the disinfection-value of each disinfectant has been ascertained by process of strict experiment, duly varied according to varying circumstances; but hitherto, even with regard to the agents which are most largely in use, experimental knowledge has been almost altogether wanting; and even the best of our so-called "disinfections" with regard to products of disease have rested rather on theories of chemical analogy than on true knowledge in the actual subject-matter.

Dr. Baxter's investigation has been intended to illustrate, with a view to more general application, the method of study which this branch of medicine requires; and with that intention, it was carefully planned by him with Dr. Sanderson. Moreover,

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* New Series, No. II.; on Filth-Diseases and their Prevention.

so far as the investigation could go (but this on a first occasion could not be very far) it has been intended to supply, in regard of certain cases, the precise experimental knowledge which is wanted as a basis for practical rules.

The agents with which Dr. Baxter has experimented are four: viz., permanganate of potash, sulphurous acid, chlorine, and carbolic acid. The morbid contagia on which the disinfection-value of these agents has been tried are three: those, namely, of vaccinia, of glanders, and of intensified (infective) inflammation; and, for reasons which are well explained in the paper, Dr. Baxter has made similar proof of each of the four agents in relation to the microzymes of common putrefaction. Within this area of experiment, some very exact results have been obtained by Dr. Baxter; and though, in our present infancy of knowledge as to contagia, we clearly are not entitled to assume that the four agents with which Dr. Baxter experimented would have in relation to all other contagia the same disinfection-values as they shewed in relation to those on which he tried them, his results may, I think, at least be regarded as highly suggestive in that wider sense, and as offering to medical practitioners far more exact clues than they have yet had towards a judicious selection and proportioning of the means with which they shall aim at disinfection.

In concluding this brief introduction to the papers which I have the honor to submit, I would beg leave, my Lords, to express my conviction that they are contributions of substantial value towards the important objects for which your Lordships are empowered by Parliament to incur the cost of the Investigations, and that both here and in other countries they will be highly appreciated in that sense by persons who themselves are engaged in giving growth to the Medical Sciences.

I am, my Lords,

Your Lordships' obedient servant,

JOHN SIMON.

Medical Department,
July 29th, 1875.

APPENDIX.

No. 1.—Dr. J. Burdon Sanderson on the Process of Fever.

The following Paper is intended to serve as a compendious statement of the knowledge which at present exists as to the nature of fever. The plan I have adopted in its preparation is in accordance with this intention. Although it would have been easier to myself, and probably more agreeable to the reader to have begun by developing in the order of time the views respecting the pathology of fever which have been so warmly discussed in this country and in Germany during the last twenty years, dealing with the facts in connexion with the doctrines which have been founded on them, I do not think that this method of treating the subject would have answered my purpose. I have therefore confined myself, as strictly as I have found it possible, to an exposition of the clinical and experimental observations which relate to the nature of the febrile process, leaving the work of combining them into a theory of fever to a future opportunity. The reader will, however, not find a mere catalogue of dry facts without connexion. I have endeavoured to follow such an order in the setting forth of the subjects treated of as appeared to me in accordance with their mutual relations, nor have I hesitated to refer to existing theories, whenever the opportunity has offered itself of pointing out the objections to which each of them is liable.

The recognised characteristics of fever are those which relate either to the disintegration of the living substance of the body or to the increase and diminished constancy of the bodily temperature. But in addition to these attributes which distinguish the febrile state of the human or animal organism from that of health, it is essential to the correct definition of fever that it should comprehend particulars relating to its origin, progress, and termination. In other words, fever is not merely a state but also a process. It has its beginning in the entrance into or action on the organism of some affecting or infecting cause. After this event, follows a period which by analogy with certain physiological processes, we are in the habit of calling the period of latency, for it is not until it is passed that the first indications within the affected or infected organism begin to manifest themselves. The state of fever once established, it may vary in its course, in its duration, and in the local inflammations which accompany it, indefinitely; but in all cases it has its onset, accession, and declension, each of which is characterised by more or less distinctive phenomena, the onset by shivering, accompanied with rise of temperature of the internal parts of the body; the augment by continued pyrexia and exhausting disorder of the bodily functions; the decline, epicrisis, or defervescence by the restoration of those processes one by one to their normal conditions and relations. The period of convalescence which follows decline, during which the mischief done is gradually compensated and repaired, and the injured organism is brought back again to its normal condition (so far as this is possible) by new growth of tissue, does not form a part of the febrile process.

These considerations afford the key to the natural division of the subject and consequently to its methodical treatment. In stating what is known as to the febrile state, I propose to study first, those facts which

relate to the disintegration of the bodily substance, and secondly, those relating to the general disturbance of bodily function of which the disorder of temperature is the chief, reserving for another opportunity the inquiry into the nature of the agents which produce fever, and the mode and limiting conditions of their action.

Part I.—Textural Disintegration in Fever.

Even to the superficial observer it is obvious that in fever the body wastes. But it is only by the scientific methods of measurement and comparison that we know how this waste takes place—how in a fevered person or animal the living substance of the body is disintegrated. This central attribute or characteristic (as it appears to be) of fever, is known partly from the study of fever artificially induced in the lower animals, partly by the observation of clinical cases. From the former source we obtain facts which are more definite, and thereby better fitted to serve as foundations for our knowledge. But the indications afforded by clinical observation, even though they may be less precise, are often of greater value, because they bring us nearer to the purpose of all pathological inquiry—the learning of the nature and causes of human ailments.

Both in the clinical and in the experimental investigation of diseased processes, measurement without comparison is useless. Thus in health, the discharge of nitrogen in the excreta is exactly counterbalanced by its introduction in food, so that it is only when this is the case that the person or animal can be said to be in a normal state of nutrition, whether the actual quantity of nitrogen which passes through the body in a given time is large or small. If in any disordered condition of health, which is under investigation, it is found that the quantity of nitrogen discharged is absolutely smaller or larger (as the case may be) than in the same individual when well, we can conclude nothing from this, unless it is ascertained at the same time how much nitrogen enters, in order that by balancing the one quantity against the other, we may learn whether the amount which is stored in the body is being wasted on the one hand, or accumulated on the other. Or, to use the ordinary and perfectly convenient language of physiology, we judge whether integration or disintegration of living substance is going on, not by the absolute income or expenditure, but by the nitrogen exchange—by the excess or defect of nitrogen expenditure as compared with nitrogen income.

Section 1.—*Experimental Investigations.*

For the best observations on the disintegration of tissue in fevered animals we are indebted to Dr. Senator, of Berlin,* on the result of whose researches the most important statements contained in this section are founded.

Senator's Researches on the disintegration of tissue in fevered animals.

The purpose of Dr. Senator's inquiry was not merely to determine the exchange of nitrogen, but also its relations with the production of heat and the discharge of carbonic acid. The method was therefore contrived and adapted with a view to these objects. As I shall have occasion in the other sections of this paper to refer to it repeatedly, I shall give the explanation of the plan of investigation so far as is necessary to enable the reader to understand it.

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* Dr. Senator's contributions to the pathology of fever have been published from time to time during the last 10 years in Virchow's Archiv. They have been recently republished under the title of "Untersuchungen über den fieberhaften "Process und seine Behandlung." Berlin, 1873.

The purpose of the inquiry being to compare the exchange of material and of heat in the febrile state with those of health, it was necessary before proceeding further, to bring the animals to be employed (dogs) into a condition of nutritive equilibrium. With this view each animal was placed for a sufficient time preceding the period of observation, on a diet of carefully-selected horseflesh, which was increased or diminished until the body-weight and daily discharge of nitrogen in urea, and the "insensible" loss became severally constant. After it had been kept on this regulated diet for some days, food was withdrawn for a period of 48 hours, during which the normal discharge of carbonic acid, water, urea, and of heat were measured. The diet was then continued as before until nitrogen equilibrium was once more established. This having been accomplished, fever was induced by the subcutaneous injection of perfectly fresh pus, and determinations of the same kind as had been previously made, were repeated *under exactly similar conditions as regards nutrition* during a second period of 48 hours. The febrile condition induced was well characterized. The temperature (as measured in the rectum) began to rise in from one to two hours after the injection of the purulent liquid, the pyrexia continuing for about two days. During the accession there were rigors, and the skin felt hot to the finger; subsequently the animals were listless and anorexic, and drank water with avidity whenever it was supplied to them.

Each experiment therefore comprised two 48 hours' periods of observation, separated from each other by an interval of several days, during which periods the production of heat, the changes of bodily weight, the daily quantities of urine and urea excreted, and the respiratory and cutaneous discharges of carbonic acid and water were determined.

The carbonic acid determinations, and the calorimetrical observations, however, related only to limited periods of measurement, each lasting an hour, repeated once or twice during the day. The "insensible loss" was computed for each period by adding the weight of ingesta to the total loss of weight in twenty-four hours, and deducting that of the excreta. As thus reckoned the result for any period of observation would, if the weight of oxygen absorbed were equal to that discharged in the form of carbonic acid, express the discharge of water and carbon from lungs and skin. As however the weight of oxygen taken in in respiration is always in excess of the weight given off, it must be borne in mind that this excess, which is a variable one, is comprised in the so-called "insensible loss." Putting this statement into the equation form:—

Insensible loss $= H_2O$ discharge $+ CO_2$ discharge $- O$ absorption.

The collection of the urine in animals is a matter of great difficulty. As regards the dog, the only method that was found to be successful is that of training the animal to empty its bladder at stated intervals. Unfortunately this cannot be done without much trouble. For the continuous collection of the products of respiration and cutaneous exhalation, the animal was placed in a ventilated chamber, which was so arranged as to answer the purpose of a calorimeter. Its construction will be described in the next section. In some instances the carbonic acid was determined volumetrically by Pettenkofer's method, in others by the balance. The water-vapour in the air discharged from the chamber was determined by weight, the apparatus for the purpose being of course interposed between the exit tube and that for the absorption of carbonic acid, so that the air reached the latter in the dry state. In most of the experiments the air as introduced into the chamber was completely saturated, so that its temperature being known, the per-centage per volume of aqueous vapour it contained could be calculated. This being the case, the difference between this per-centage and that of the outflowing air gave the quantity of water exhaled by the animal. It was recognised, however, by Dr. Senator that this determination was not exact, for of the out-going water-vapour much must have been lost by condensation on the wall of the chamber. Considering that in fever the natural ingestion of food is reduced to a minimum, it is obvious that any comparison made between an animal normally fed, and a

fevered animal, would give no exact information. For even if the nitrogen value of the food taken by the animal in the febrile state were accurately determined, no precise estimate of the weight actually assimilated could be founded on it. In health we can do this with precision; for as soon as the physiologist finds by the constancy of the weight of the animal, that the income and expenditure of material balance each other, he knows that the expenditure is a true index of the activity of the nutritive process. But in artificial fever, from the short duration and the variableness of the conditions to be investigated, no such balance is attainable; so that it must always be quite uncertain in the case of an animal which is still digesting a greater or less quantity of food, how much of the nitrogen it discharges is derived from income, and how much from store. In Dr. Senator's experiments the only available method of securing accuracy was adopted. It consisted in observing the same animal after it had been brought to normal equilibrium as above explained, during two successive periods of inanition, separated from each other by an interval, during which the animal was fed as usual, and again brought to nutritive equilibrium.

In the following table I have brought together the results of a long series of these observations, so far as they relate to the discharge of urea and carbonic acid:—

TABLE I.

Showing the Results of Quantitative Determinations of Urea and Carbonic Anhydride discharged respectively by a Normal Animal, and by the same Animal in the Febrile State during successive Periods of Inanition.

	Bodily Temperature in rectum. (Means.)	Discharge of Carbonic Acid in one hour of Observation.	Discharge of Urea in 24 hours.
Experiment 1. Weight of animal, 11 lbs. 10 oz.			
1st Day Normal	39·0	3·6	6·01 Grammes
1st Day Fever	39·3	3·4	9·0
2nd Day Normal	39·0	3·3	No Observation.
2nd Day Fever	40·3	3·7	Do.
Experiment 2. Weight, 13 lbs. 4 oz.			
1st Day Normal	39·1	4·03	
1st Day Fever	39·4	3·93	
2nd Day Normal	39·1	4·78	No Observation.
2nd Day Fever	40·3	4·02	
Experiment 3. Weight, 16 lbs.			
1st Day Normal	39·0	2·88	7.89
1st Day Fever	39·6	2·73	14·48
2nd Day Normal	38·8	2·72	No Observation.
2nd Day Fever	40·7	4·20	
3rd Day Fever	40·7	3·77	
Experiment 4. Weight, 10 lbs. 10 oz.			
1st Day Normal	39·3	2·72	6·39
1st Day Fever	39·5	2·75	10·27
2nd Day Normal	39·3	2·45	
2nd Day Fever	40·7	2·88	No Observation.
3rd Day Fever	39·6	2·91	
Experiment 5. Weight, 9 lbs. 2 oz.			
1st Day Normal	38·9	2·38	6·87
1st Day Fever	39·7 40·3	3·09	11·47
2nd Day Normal	38·9	2·20	4·61
2nd Day Fever	41·0	2·07	No Observation.

		Bodily Temperature in rectum. (Means.)		Discharge of Carbonic Acid in one hour of Observation.		Discharge of Urea in 24 hours.
Experiment 6. Weight, 24 lbs.						
1st Day	Normal	39·0		5·39		10·0
	Fever	39·2		4·38		17·1
2nd Day	Normal	39·6		5·44		8·1
	Fever	40·0		6·47	6·22	10·91
Experiment 7. Weight, 12 lbs. 3 oz.		Morning.	Afternoon.	Morning.	Afternoon.	
1st Day	Normal	38·8	38·8	3·59	4·02	8·86
	Fever	38·7	40·7	2·58	3·26	13·95
2nd Day	Normal	38·8	38·6	4·09	3·31	7·9
	Fever	40·0	40·0	3·13	3·58	9·47
3rd Day	Fever	40·4	39·9	3·07	2·79	No Observation.

In this table the approximate weight of the animal to which each experiment refers is stated in the first column. The term "first day" expresses a twenty-four hours period of observation, commencing in each case twenty-four hours after the last feeding. In the same horizontal line with the word "normal" in the second column are set down, first the temperature of the animal (derived usually from several observations) during the first day of comparative inanition without fever; secondly, its discharge of carbonic acid, measured either during one period of one hour's duration, or during several such periods, as in Obs. VII.; and, lastly, its discharge of urea as measured during the whole twenty-four hours. In the second line, opposite the word "fever," the same particulars are registered in the same order as regards the same animal in the same stage of inanition, but in the febrile state. In the two lines following, the observations relating to the second day of inanition are recorded in a corresponding manner.

The tabular arrangement renders it possible to comprehend at a glance the general bearing of the results. It is seen at once that, although the febrile state as indicated by the temperature, as well as by the general condition of the animal, was thoroughly established, its effect on the rate of discharge of carbonic acid was very inconsiderable. In five, indeed, out of the seven cases, it appeared to exercise no appreciable influence in either direction, and in the other two, although there was during the second day a slight augmentation, it was trifling in amount.

Results of Dr. Senator's researches.—Discharge of nitrogen.

As regards the excretion of urea, the indications afforded by the results are set forth by Dr. Senator, to the following effect: *—As has been already shown by the investigations of Naunyn,† the febrile augmentation of the urea discharge takes place immediately after subcutaneous injection of pus, *i.e.*, at a time which precedes the elevation of temperature. In observation VII., in which the urine was collected, and its quantity and urea per-centage estimated during the first eight hours after injection, it was found that there was already a very marked increase of both, so that, while, as will be seen later, the discharge of heat, of carbonic acid, and of aqueous vapour, may even be diminished during the initial stage of fever, that of urea is augmented. In the later stages this relation is in the main reversed, all discharges and par-

* Senator, l. c., pp. 59, 60.

† Berliner klinischer Wochenschrift, 1869, March 15

ticularly the "insensible loss" as indicated by the rapid loss of weight, being decidedly increased. In association with this, the urea discharge "remains excessive during the whole course of the fever," while the rate of discharge of urine increases so markedly towards the end of the first day, that, notwithstanding the diminution which is the immediate consequence of the injection, the quantity for the 24 hours is in excess.

Senator further draws attention to the very remarkable fluctuations and inequalities which all the functions investigated exhibit when they are continuously observed. This is seen to be true, not merely of the rate of discharge of urea and carbonic acid, but more strikingly of the loss of weight. When the weighings are repeated at short intervals, it is found, that whereas at one time the loss is scarcely to be estimated, at another it is three or four times as great as that which occurs in health during the same period.

Increased discharge of urea in induced fever is not dependent on accumulation.

The increase of urea discharge in artificial fever cannot possibly be dependent on the excretion of urea which has previously accumulated in the blood or tissues, for, from the well-established fact that in those tissues which constitute the greater part of the weight of the body, viz., muscles and bones, urea is entirely absent, and that in those organs in which it is most abundant, *e.g.*, the liver, its per-centage never exceeds 0·02 — 0·03, it is clear that even if the whole quantity stored in the body were discharged at once, the effect on the rate of discharge would be barely perceptible. It is therefore obvious that, in the dog at least, its augmentation in the urine is an indication of increased activity of those processes by which it originates in the body, and that the degree of that increased activity may be judged of pretty correctly by the rate of discharge. As, therefore, we are certain that urea derives its nitrogen from albumin, we are also certain that, at all events in artificial fever, albumin of some kind is disintegrated in greater quantity than in health.

Discharge of carbon. Reasons for inferring that if a comparison were made of the carbonic acid discharge of the fevered animal body and that of the normal at the same temperature, it would be found to be greater in the latter.

So far as the frequently ventured assumption goes that in fever the discharge of carbonic acid is necessarily increased, these results go a long way towards negativing it. They have no value, however, as evidences that the carbonic acid discharge is diminished, although from a number of considerations it seems highly probable that it is so. For in the experimental comparison of fever with health, it is to be borne in mind, that however exactly you may assimilate the conditions of observation, there is one important condition which, while it appears to belong to the organism, belongs in reality to the environment, viz., that of temperature. The temperature of the body, although it is a direct consequence of the chemical processes of life, may from another point of view be quite as correctly regarded as their cause, or at all events as a modifying condition, for the very increase of heat which fever produces, reacts on and influences the fevered body. Consequently, in experiments made on Senator's plan, even when the utmost has been done to render the two observations strictly comparable, the living tissue is not really under identical conditions, for every bit of living protoplasm is acted upon by the general pyrexia, just as if heat were communicated to it from outside. Now we know that when heat is communicated to the body from surrounding media, so as to elevate its temperature even very slightly, the effect of such slight elevation is to produce a very considerable augmentation of the discharge of carbonic acid, and that this effect is rapidly increased as the temperature communicated to the body approaches that of pyrexia. It is, indeed, quite possible, that if in Senator's observations the comparison had been made between normal and fevered animals at the same bodily temperature, it would have been found that the carbonic acid discharge in the former would have been largely in defect. Comparative observations of this kind have not yet been made, but in the mean time we need have no hesitation in adopting Senator's conclusion, that there

is no reason for believing that in induced fever in the dog, there is any increased formation of carbonic acid in the body.

From the observations relating to the quantity of urine and from the loss of weight, Senator concludes that the discharge of water is very considerably increased in fevered animals. He attributes the increase in the quantity of urine partly to the presence of an excess of urea in the blood, (which, as Ustimovitsch's experiments have shown, acts diuretically,) partly to the state of the circulation, and (during the rigor) to the suppression of the exhalation of water from the skin. As the febrile process advanced, the rapid loss of weight, (which the carbonic acid determinations during the same period showed not to be attributable to the augmented discharge of that product,) indicated a much increased insensible perspiration, so that we must suppose that during the later stages both channels for the discharge of aqueous vapour are wide open. Here, however, as in the case of the carbonic acid discharge, no ground whatever is afforded for the assumption that a greater production of water by oxidation takes place than in health, for there is reason for believing that the direct influence of increased temperature in favouring the exhalation of water is even greater than that which it exercises on the discharge of carbonic acid. On this point again, positive observations are wanting.

Discharge of water in induced fever.

The results of Senator's observations relating to the loss of weight in fever and health respectively may be stated as follows :—Fevered dogs lost on the whole from 3 to 4 per cent. of their weight during the first 24 hours of fever. Healthy dogs, in the corresponding period of inanition, lost about 1·6 per cent. As there was certainly no increase of carbonic acid discharge, this must have been chiefly due to loss of water.

Section 2.—Clinical Investigations.

It is obvious that the investigation of the exchange of material in fever is much more difficult in man than in the lower animals. This difficulty arises chiefly from the absence of any normal standard with which the condition of the fevered body as regards its income and expenditure can be compared. Just as it was necessary, in the experimental inquiries to which the last section relates, in order to value the results observed in the febrile state to place them side by side with corresponding results relating to animals under precisely similar conditions, fever excepted, so here it is equally plain that if we desire to interpret justly whatever measurements we may be able to make of the physiological products of the human organism under the influence of fever, this can only be done by first ascertaining how much of each product would be yielded by an individual of the same weight under the same circumstances. A patient in fever is in bed and motionless. The food he takes is, as regards the quantity of albuminous material it contains, a mere fraction of his ordinary diet. The first question to be answered in approaching the subject of this section is—What quantities of urea and of carbonic acid ought a normal person in health to discharge from his body when in bed and on fever diet ?*

Discharge of nitrogen.

The basis of fact on which it is possible to found an estimation of the normal discharge of urea by a healthy individual when on fevered diet

* It is remarkable how frequently this fundamental consideration has been neglected in the discussion of clinical observations on fever. Some clinicists are content with a vague notion that in health something like 500 grains of urea are excreted daily, and that if the febrile discharge is greater than this, it must be excessive, and vice versâ, forgetting that, unless by some means or other the influence of diet is estimated, the mere determination of the daily discharge of urea is of no value whatever.

and in bed, is unfortunately very limited. Indeed, the only observations on the subject which are available, are those made by Dr. Unruh* on three patients in Professor Leyden's wards at Königsberg in 1869. The patients in question were affected with non-febrile diseases. The first, a cabman aged 47, suffering from carcinoma ventriculi, weighed 104 lbs. His diet consisted of beef tea or broth, with an egg or two. The quantity was probably excessively small, for the daily discharge of chloride of sodium scarcely exceeded one gramme. He was under observation 19 days, during which his temperature was normal, and the specific gravity of his urine was natural. The mean daily discharge of urea was 17·5 grammes. In two other patients affected with syphilis, each of whom was observed during 13 days, the daily means of urea were severally 18·58 and 16·267, both being on fever diet with milk. Thus we have 17·466 grammes(=270 grains) as the mean of the three observations; or 0·3835 gramme per kilo. of body weight; whereas the normal excretion of urea per kilo. is about half a gramme. The mean discharge of uric acid in the first case was 0·009 per kilo. per diem.

Having obtained this basis, Dr. Unruh proceeded to investigate in a similar way cases of different kinds of febrile disease, of which the results will be found stated in a long series of tables in his mémoire. They are summed up by him as follows:—

Assuming that 0·38 grammes per kilo. per diem (=2·68 grains per lb.) represents sufficiently accurately the normal low diet discharge of urea in health, he found that in one case of relapsing fever, with an evening temperature of 40°·8 C. (105°·4 F.), and a morning temperature of 38°·2 (100°·76 F.), the discharge was on one occasion as great as 65·97 grammes i.e. 1·18 per kilo. per diem, more than three times the normal, this being the highest result obtained. The lowest amount in a case of pneumonia (with a history of previous chronic disease) was 18·6 per diem, which is scarcely above the normal. This condition presented itself only during the first few days of observation. The general result of the whole series was that the normal urea discharge per diem in intense fever may be set down at 30·576 grammes (= about 470 grains,) hence, something like one and a half times as much as would be discharged by a healthy person on fever diet.

Dr. Senator thinks this estimate too low, on the ground that in most of the cases the beginning of the febrile process was not included, and consequently that during the period of observation, the patient having been previously subjected for a length of time to the combined influence of inanition and fever, was already exhausted of his store albumin, so that Dr. Unruh's mean could not be regarded as a fair one; and refers in support of his view to the published urine analyses of Moos and Rosenstein in typhoid and typhus, both of which show that the urea discharge is larger at the very beginning of the attack than it is afterwards. Unfortunately, the number of cases in which the urea discharge has been observed from the beginning to the end, is exceedingly small. Dr. Senator has been able to meet with only two, one observed by himself, the other by Dr. Wachsmuth, which were complete in this respect. He has, however, brought together 13 selected cases in which the observations were begun sufficiently early, and in which the significance of the results was not impaired by any conditions affecting the patient. He has divided these 13 cases, which must be regarded as by far the most important body of clinical evidence which exists on the question of the exchange of nitrogen in fever, into categories

* Unruh, Ueber die Stickstoffausscheidung bei fieberhaften Krankheiten: Virchow's Archiv., vol. xlviii. p. 227.

according to the presence or absence of collateral circumstances which might be supposed to affect the discharge of urea. By doing so, he has been able to estimate the influence of each such condition separately, and thus to add weight to the general conclusions.

One of the most important of these circumstances relates to the previous nutritive condition of the patient. In Voit's well-known observations on inanition, it was found that the time required for the production of a given effect on the exchange of material in any animal varied according to the store of albumin existing in the body, so that *e.g.*, an ill-fed dog was in the same condition after 24 hours as a well-fed after five or six days The same thing holds good in clinical practice: here, as there, it makes a great deal of difference whether the patient enters into fever with his body well supplied with nutritive materials or not, *i.e.*, whether his previous diet has been abundant or indifferent. The first category includes therefore the two cases above referred to, in which it was not only possible to observe the febrile process throughout, but to ascertain the nutritive antecedents with exactitude.

1. Case observed by Dr. Wachsmuth* :—Pneumonia in a male, with temperature varying from 40° (104° F.) to 41°2 (106° F.). The patient, who during the first three days took no nourishment, and during the last two days only milk, excreted in the five days, which comprised the whole of febrile period, 206·44 grammes of urea, *i.e.*, 41·3 grammes daily.

2. Case observed by Dr. Senator in the Charité :—J. H., a male nurse, æt. 25, tolerably robust, took ill on the 16th of February 1870, with relapsing fever. On the following day the temperature had risen to 40°·5 C. (104°·9 F.) the highest point reached. In the course of the 21st, critical defervescence took place, which was accompanied by profuse sweating, lasting over the following day. Up to this time his daily nourishment consisted of from 1,000 to 1,200 cubic centims. (about two pints) of soup, and 400 to 600 cubic centims. of milk. During the six days of the fever, he excreted 240·73 grms. of urea, *i.e.*, 40·1 grms. per diem.

In the case of Dr. Senator's patient, who was a male nurse in the Charité, it was quite certain that the nitrogen value of his previous diet did not correspond to more than about 25 grammes of urea. The other was also an under-fed individual. In each case the febrile condition was over in less than a week ; so that the period during which the patients were under observation overlapped that of the duration of fever. The patient was on a diet containing a mere trace of nitrogenous material. The daily quantity of urea as compared with the normal inanition daily discharge above estimated (17 grammes) gives 126 per cent. as the febrile increase.

The second category comprises four cases in which the previous nutrition was similar, but the observation was not begun until two or three days after the accession.

1. Case recorded by Dr. Huppert† :—Pneumonia in a male, whose highest temperature was 39°·9 (103°·8 F.). Quantity of urea discharged between the second and seventh day, both included, 200·69 grammes, *i.e.*, 33·5 grammes per diem.

2. Case observed by Pribram and Robitschek‡ :—Relapsing fever in a male, aged 28. Highest temperature recorded 40°·4 C. (104°.72 F.). Between the second and fourth day of his illness he excreted 168·3 grammes of urea, *i.e.*, 56·1 grammes per diem.

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* Wachsmuth (quoted by Huppert), Archiv der Heilkunde, Vol. VII.

† Huppert, Ueber die Beziehung der Harnstoffausscheidung zur Körpertemperatur im Fieber. Arch. der Heilkunde, vol. vii. p. 1.

‡ For the case of Pribram and Robitschek, Dr. Senator refers to the Prager Vierteljahrschrift for 1869.

3. Case observed by Huppert :—Pneumonia in a male, aged 18, who during the four days following the third of his illness had febrile temperature varying up to 40°·75 C. (105°·3 F.) and took no solid nourishment. The observation was interrupted before the crisis. In the four days he excreted 138·2 grammes of urea; *i.e.*, 34·5 grammes per diem.

4. Case observed by Huppert and Riesell* :—Pneumonia in a male, aged 25. During six days of "high fever," from the third to the eighth day of his attack, both included, the total weight of nitrogen in the nourishment consumed by him amounted to 2·97 grammes, while nearly twice as much was discharged by the alvine evacuations and sputa. In the six days he excreted a quantity of nitrogen by the urine, corresponding to 223·6 grammes of urea; *i.e.*, 37·2 grammes of urea per diem.

Mean daily discharge of urea in the four cases, 40·3 grammes.

Here, again, the mean of the results gives about 124 per cent. as the fever increment, showing that the exclusion of the first day or two had no great influence. But in the third category, comprising cases in which the illness was of longer duration, and the observations related to a more advanced period, the mean urea discharge was only 34·5 grammes, and the increment was therefore 98 per cent.

1. Case observed by Unruh (loc. cit. p. 242) :—Pneumonia in a male aged 21, weighing 122 lbs., whose temperature rose during his attack to 40°·5. (104°·9F.) During the seven days of his illness, beginning with the third and including the crisis, 278·47 grammes of urea were excreted; *i.e.*, 39·8 grammes per diem.

2. Case observed by Huppert (loc. cit. p. 25) :—Acute rheumatism with heart complication, in a male aged 21, weighing 130 lbs. Temperature during the first 10 days from 38° to 40°. During this period the patient's diet consisted of a variable quantity of milk, with the addition during the first two days of a little soup and bread. On two of the following days no food was taken. The excretion of urea during the 10 days amounted to 394·67 grammes; *i.e.*, 39·4 grammes daily.

3. Case observed by Wachsmuth (reported by Huppert, loc. cit.):—Pneumonia in a male, whose highest temperature during the attack was 40°·5. C. (104°·9 F.) Between the second and the eleventh day, during which period the patient took nourishment, he excreted 231·9 grammes of urea; *i.e.*, 23·2 grammes per diem.

4. Case observed by Salkowski†. Erysipelas in a youth of 18, in whom the highest temperature was 40°·2. (104°·4 F.) He was on fever diet from the 3rd to the 12th day. In eight days he excreted 319·44 grammes of urea, *i.e.*, 39·9 grammes per diem.

5. Case observed by Pribram and Robitschek (loc. cit.) :—Relapsing fever in a young man of 22. Highest temperature recorded 40°·4. (104°·7 F.) In the eight days, from the 3rd to the 10th day of the illness, during which the daily diet consisted of soup and a gill of milk, he excreted 218·67 grammes of urea; *i.e.*, 27·3 grammes per diem.

6. Case observed by Senator :—Pneumonia of the right upper lobe in a very robust and well-nourished journeyman slaughterer, aged 24. The patient, who had shivered on the 2nd of March, was admitted into hospital on the 4th. On the 5th and 6th his temperature reached 40°·5. (104°·9. F) On the 8th defervescence took place. During the seven days, from the 3rd to the 9th, inclusive, his diet consisted of soup, coffee, and 600 cubic centims. of milk daily; and he excreted 225·10 grammes of urea, *i.e.*, 37·5 per diem.

It is to be noticed that the cases selected were of very various diseases, diseases, in short, which have nothing in common, except the febrile state.

The general conclusion to be derived from the whole series is that in the early stage of fever a patient excretes about three times as much urea as he would do on the same diet if he were in health, the difference

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* Huppert und Riesell, Ueber den Stickstoffumsatz beim Fieber. Arch. der Heilkunde, vol. x. 1869, p. 329.

† Salkowski, Untersuchungen über die Ausscheidung der Alkalisalze. Virchow's Archiv, vol. Liii. p. 209.

between the fevered and the healthy body, consisting chiefly in this, that whereas the former discharges a quantity of nitrogen equal to that taken in, the latter wastes the store of nitrogen contained in its own juices. That this disorder of nutrition is an essential constituent of the febrile process is indicated by the fact that it not only accompanies the other phenomena of fever during their whole course, but precedes the earliest symptoms and follows the latest. That it anticipates the beginning of fever was first demonstrated by Dr. Sidney Ringer * in his investigation of the relation between temperature and the discharge of urea in ague. That the same condition continues after the crisis has past, *i.e.*, the temperature has begun to sink, has been shown by Dr. Squarey from his investigation of eighteen cases of typhus, in all of which the daily excretion of urea was measured, and the variations of temperature were observed during the whole course of the disease, and the observations were continued until convalescence was completely established. In these cases it was found that, whereas the bodily temperature which in this disease rises rapidly at the beginning, and keeps up without sensible abatement during a period which often extends to the middle of the second week, usually begins to fall after the tenth day, the daily rate of discharge of urea, although usually above the normal during the first week did not attain its maximum until the temperature had been falling for some days.†

The question of the source from which the urea increment of fever comes is one which can be better discussed subsequently. At present it is sufficient to notice that the anticipation of the obvious symptoms of illness, particularly of the pyrexia, by the increased excretion of urea, as well as the continuance of the urea excess during the epicritical period, plainly indicate that pyrexia is not the agent by the direct influence of which the increased secretion of urea is produced.

Another consideration suggested by the same facts is this, that the mere increase of the per-centage of urea discharged, affords an inadequate measure of the waste of nitrogen, *i.e.* of albumin, which actually occurs in fever; for to form a just estimate, the overlapping at both ends of the process ought clearly be taken into account. Moreover, in fever there are very frequently losses of nitrogen by the bowels and skin, as well as by exudations, the amount of which scarcely admits of being determined.

It having been established that there is an increased discharge of nitrogen in fever it remains to state what is known as to its source. There are two sources which are open to discussion, viz.: (1) the albumin of the blood and lymph, and (2) that of the tissues; or, to use the expression which the researches of Voit have rendered current in physiology, store albumin, and tissue albumin. By the former we understand the albuminous constituents of the corpuscles and plasma as well as of the tissue juice or lymph; by the latter, the material of protoplasm, including that of the blood corpuscles.

Here the basis of observation is furnished by researches made by Dr. Salkowski, relating to the proportion of potassium salts discharged

* On the connection between the heat of the body and the excreted amounts of urea, chloride of sodium, &c., during a fit of ague. Medico-chirurgical Transactions, vol. XLII. p. 361. In this paper Dr. Ringer recorded more exact observations than had before been made as to the relation between the temperature and the other phenomena of the paroxysm of ague. In the course of them he made the important discovery referred to in the text, viz: that in this disease the augmentation of the urinary discharge of nitrogen not only begins some time before the accession of the cold stage, but even precedes the rise of temperature.

† Observations on the temperature and the urine in Typhus fever. Medico-chirurgical Transactions, vol. L., p. 329.

by the urine in fever, as compared with that of sodium salts. These researches relate to some twenty cases of various forms of febrile disease in Professor Leyden's wards at Königsberg. The research began with an investigation of the relative proportions of potassium and sodium salts discharged by the liquid and solid excreta in health, the observer being himself the subject of observation. The diet being mixed, and the nutritive condition nearly that of nitrogen equilibrium as seen by the constancy of the daily discharge of urea, (min. 25·3, max. 27·2, mean of seven days 25·69) the daily quantity of potassium and sodium salts respectively, reckoned as potash and soda were: potash, 3·094 grammes, soda, 4·207 grammes; so that of the sum of both alkalies potash constituted 41·4 per cent.

In another individual, a clerk, on low diet without meat, affected with syphilis but in good general health, the soda discharge was about the same, but that of the potash much less, so that the potash per-centage varied from 18 to 26. From these and other observations it was concluded that the daily potash discharge of a healthy person on fever diet is less than one gramme.

The febrile cases investigated were one of relapsing fever, one of erysipelas, and several of pneumonia. In the case of relapsing fever, which was observed during part of the first paroxysm, the whole of the first remission, and of the first relapse and second remission, it was most distinctly seen, that whereas during the remission, the potash per-centage of the total discharge of both alkalies sank to about 18·20, it rose during and especially after each crisis to about 90. In the case of erysipelas and in the pneumonia cases there was a corresponding relative and absolute increase of the potash discbarge. There were however, peculiarities in all the cases which have been fully described by the authors, and are of sufficient importance to require notice.

On the whole the absolute quantity of potassium discharged on febrile days, is three or four times as great as on non febrile. As regards soda the results are entirely different. During fever it is seen in most of the tables that the soda discharge is extremely low. As soon as the crisis is passed it at once begins to increase to such an extent that in one day as much soda is eliminated as on all the previous days taken together. Simultaneously the per-centage of potash discharge falls to its lowest.

The augmentation of potash discharge in fever, when little or no meat is being taken, and its rapid decline in defervescence shows that the augmented production of urea in fever must take place at the expense of some source of albumin which contains potash. We have, therefore, in this fact an answer to the question from which we started. The albumin which serves as a source of urea in fever, is not derived from liquor sanguinis, (for the liquor sanguinis abounds in sodium salts, but contains very little potassium,) but either from the blood corpuscles, or from muscle or both.

The very remarkable diminution of the discharge of sodium signifies of course that in fever, the common salt, which constitutes the bulk of the salts of the blood, is retained; for immediately after the crisis, (as shown most distinctly in three of the cases,) it passed into the urine in great abundance.

In addition to increased excretion of potash there is another circumstance which points to the blood corpuscles or to the muscular tissue as the chief seat of disintegration in fever, namely, the increased discharge of colouring matter. Unfortunately as regards this most important question sufficient information is wanting. There are, to the best of my knowledge, no comparative determinations either of the proportion

of blood corpuscles or (what would be as useful) of the iron per-centage of the blood before and after acute fever either in man or in the lower animals. The only facts relating to the subject that I know of are (1) that in all febrile diseases, the colouring matter of the urine, which is probably derived ultimately from the blood hæmoglobin, is three or four times as abundant as in health (*see* Neubauer and Vogel); and (2) that after traumatic fever in dogs, there is a very marked diminution, both of the corpuscles and of the iron of the blood. But these observations are quite inadequate to serve as a basis for an opinion as to the proportion which the breaking down of blood corpuscles bears to the total disintegration of fever. Of the many questions which require answering, there is perhaps none which is of greater importance, for if, as appears probable, the destruction of the coloured corpuscles is a part of the febrile process, the fact must have a very important bearing, not merely on the process itself, but on its after results. The colouring matter of the blood being the means by which oxygen is distributed to the tissues, the destruction of it must impair every function of organic life.

Discharge of carbonic acid in fevers.

As regards the exhalation of carbonic acid in fever, the existing knowledge is much more unsatisfactory than that which relates to the disengagement of nitrogen. Indeed, the only observations on the subject are those of Prof. Leyden.* Their very great importance renders it necessary to give an account of them.

Leyden's observations, although perhaps insufficient in number, were made with an exactitude and completeness approaching more nearly to scientific experiment than any clinical researches with which I am acquainted. Above all, they have the singular merit of being comparative, *i.e.*, that in each case the measurements of carbonic acid discharge in fever were valued, not by a standard derived from averages of observations made on other persons, but by control measurements of the same function in the same individual when in health. Another point of very great importance is that the urea discharge is estimated during the same periods as the carbonic acid discharge, the comparison of the fluctuation of the two functions adding materially to the certainty and value of the results.

The observations were made on four cases, viz., two of relapsing fever, one of typhus, and the other of pneumonia. In the two cases of relapsing fever the quantity of air respired per minute, (one of the patients being a male, æt. 63, the other a female, æt. 20) was on the whole 50 per cent. greater than during the interval of apyrexia, the observation being made in the first case before and during the first remission, in the second during the whole of the first remission as well as during the first relapse and the second remission. In the second case the contrast between the febrile and non-febrile days was extremely striking. Thus in the morning of Jan. 23, the last fever day of the first relapse, when the temperature was 40°·1 (104°·2 F.), and the frequency of breathing 34 per minute, the quantity of air respired per minute was 8·13 litres, and the per-centage of carbonic acid contained in it 3·28. In the evening the temperature had fallen to 36°·8 (98°·2 F), and on the following day (Jan. 24) the temperature was 36°·6, and the rate of breathing 24. It was then found that the respiration per minute was reduced to 4·85 litres, the per- centage being increased to 3·8.†

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* Leyden. Ueber die Respiration im Fieber. Deutsches Archiv für klinische Medicin, Vol. VII., 1870, pp. 536–562.

† *See* p. 549 and *seq.*

In the third case, which was one of typhus complicated with hypostatic pneumonia, the most important peculiarity was that during the time that the dyspnœa consequent on the pulmonary affection was most marked, although the temperature had subsided and was nearly normal, the quantity of air breathed was large (10·72 litres per minute), and the per-centage very low. Dr. Leyden has divided the observations relating to this case, which commenced at the maximum of the pyrexia, and were continued through the period of defervescence, and the beginning of convalesence, into three parts. In the first, relating to a period during which the temperature ranged from 39°·6 to 40°·1 (103°·3 to 104°·2 F.), the patient breathed 11·7 litres, with a per-centage of carbonic, acid of 2·26, the frequency of breathing being 40 per minute; in the second, with a temperature varying from 37° to 39° (98°·6 to 102° F.), (the rate of respiration being still frequent with some dyspnœa) 9·8 litres were breathed, with a per-centage of 1·76; in the third, with perfectly normal temperature and respiration at 22, 6·66 litres, containing 2·8 per cent. of carbonic acid, were expired. Consequently the total discharge of carbonic acid per minute was greater during convalescence than in the epicrisis, notwithstanding the diminished quantity of air respired, in the proportion of 28 to 26. In the fourth case, one of pneumonia, the effect of dyspnœa in increasing the quantity of air breathed is still more marked. Here the observation was commenced at the height of the disease, when the temperature was 40°·5 (104°·9 F.), the pulse 120, and the respirations were 44 to 48. The patient breathed 9·0 litres, containing 3·05 per cent. of carbonic acid. On the next day his temperature was reduced to 39°·1, his pulse to 104 in the morning, and to 84 in the evening, his respirations to 36 (morning) and 26 (evening). He respired only 6·8 litres with the same per-centage. During the four following days when convalescence established itself, the quantity gradually sank to 3·72 litres, while the per-centage increased, but by no means in the same proportion, the highest being 3·45.

Dr. Leyden sums up the results of the four cases as follows:—

	Febrile period.		Non-febrile period.	
	Quantity of air respired, in litres, per minute.	Per-centage of Carbonic Acid.	Quantity of air respired, in litres, per minute.	Per-centage of Carbonic Acid.
Case 1 - - - -	8·76	3·15	6·146	3·4
„ 2 - - - -	7·526	3·79	5·146	3·8
„ 3 - - - -	11·69	2·26	6·66	2·8
„ 4 - - - -	7·912	3·05	4·492	3·2

Hence we have as the general results of his investigation an increase of from 50 to 75 per cent. of the quantity of air breathed per hour, and a diminution of about 10 per cent. in the carbonic acid. Combining these, we have the febrile augmentation of the carbonic acid discharge amounting to nearly 50 per cent.

Before we accept these facts as evidence that increased discharge of carbonic acid is a characteristic of fever, it is necessary here, as with respect to the discharge of nitrogen, to satisfy ourselves that they are not directly consequent on functional disorders, which, although present in the cases observed and often associated with fever, are unquestionably

not of its essence. Physiologists are aware that any abnormal elevation of bodily temperature, whether produced by interference with the discharge of heat from the surface, or by exposure to an external temperature above the ordinary limits of variation, determines an increased disengagement of carbonic acid. It is also known that this augmentation is associated with increased activity of respiration, but it has not yet been shown whether, on the one hand the increased liberation of carbonic acid is entirely accounted for by the greater frequency and depth of the respiratory movements, or on the other is dependent partly on this cause, but partly also on the increased activity of those chemical processes of which carbonic acid is the product. In other words, it is known that the animal body gives off more carbonic acid when its temperature is slightly elevated above the normal, but it is not yet known whether it produces more.

As regards fever, we are nearly, but not quite, in the same position. In many febrile diseases, no doubt, the increased disengagement of carbonic acid is at first the result of more active respiration, but this explanation cannot apply to any instance in which the fact is observed for more than a few hours. The only way in which increased respiration can produce increased discharge of carbonic acid is by furthering the disengagement of whatever quantity of that body was previously accumulated, an effect which can last only a limited time. We are, therefore, compelled to accept it as a fact that in fever more carbonic acid is actually formed in the body than in health.

General view of the exchange of material in fever.

We are now in a position to take a general view of the febrile process, so far as relates to the exchange of material and the disintegration of tissue. We have seen that it is established on grounds which do not admit of any question, that a fevered man or animal discharges more nitrogen than a healthy person or animal on the same nitrogen income; and, that as regards man, the febrile excess amounts to something like three quarters of the normal expenditure. We have also seen that in man there is during fever an excess of discharge of carbonic acid, and that this cannot be accounted for as the mere result of excessive respiration, but that no such excess is observed in the dog. We have now to bring these facts into relation with each other.

In health, the whole of the nitrogen discharge is derived from food. In inanition, when nitrogen income vanishes, all the nitrogen which passes out as urea or otherwise is derived from stored or tissue albumin. In fever this is also the case, for the nitrogen income is as defective in the one condition as in the other, but besides the using up of stored albumin, there is an additional and altogether abnormal disintegration which, for reasons already stated, we believe to take place at the expense of blood corpuscles, of muscle or other tissue. That fact must be taken as a starting point in any attempt to understand the febrile process as a disorder of nutrition.

A healthy adult on ordinary mixed diet discharges from 30 to 36 grammes of urea daily; a healthy adult, on fever diet, discharges from 15 to 20 grammes; but if he is fevered he discharges, on the same diet, a little more than on ordinary diet in health, say from 35 to 40 grammes. A normal person on fever diet discharges about 22 grammes in an hour, of carbonic acid, in health, about 32·3 grammes in fever. Where does this come from?—To account for the urea excess, one must suppose, (the nitrogen equivalent of one gramme of urea being three grammes of albumin,) that sixty grammes of albumin is disintegrated in 24 hours. These 60 grammes would (the carbon per-centage of albumin being 53) contain 31·8 grammes of carbon of which one fifth of the weight of urea discharge, (the proportion of carbon in any given weight of urea

being $\frac{12}{60} = \frac{1}{5}$,) *i.e.*, four grammes would pass out as urea. The remainder, viz., 27·8 would leave the body in 24 hours in the form of carbonic acid. Now 27·8 grammes of carbon correspond to 102 grammes of carbonic acid, which would therefore express the increase of carbonic acid discharge which would result supposing that all the carbon of the tissue disintegrated to form the febrile excess of urea, left the body in that form. 102 grammes per day is only $4\frac{1}{4}$ grammes per hour; consequently the quantity of carbonic acid produced by the disintegration of albumin in fever is a mere fraction of the total quantity exhaled (32·3 grammes). We have therefore a remainder of 28 grammes which must be derived from the consumption in the body of material not containing nitrogen. The bearing of this fact on the question of febrile thermogenesis will be considered in the next section.

Part II.—Production and Discharge of Heat in Fever.

Section 1.—*Experimental Investigations.*

The constancy of the temperature of the body depends upon the existence of heat equilibrium, *i.e.*, of that condition of the organism in which the processes by which heat is produced, and those by which it is liberated, balance each other. It is certain that increased activity of the former is not in itself a sufficient cause for high temperature, for we know that the thermogenetic functions undergo frequent variations, some of which are accidental, while others take place regularly, without the occurrence of any corresponding changes in the temperature of the body. Thus after a meal, a variety of heat-producing processes come into operation, which were before in abeyance; again, during and after muscular exercise the quantity of material disintegrated is much greater than in repose; but in neither instance is there any permanent elevation of the bodily temperature, because in both the increased production is balanced by the increased liberation of heat at the surface. In like manner it can be shown that an unnaturally high temperature may be maintained although the production of heat is diminished. Thus, it is well known that after certain modes of death, the temperature of the body does not sink for some time after the circulation has ceased, notwithstanding that the heat-producing processes which are dependent on the supply of oxygen are no longer in operation.

Heat stands on the same line with carbonic acid, urea, and water, as a product of chemical work done in the living body. To determine whether or not its production is increased or diminished, we have to proceed by continuous measurement just as in the other cases, with this difference, that the measurement of heat is a much more complicated and difficult problem than that of any of the chemical products of life. There are two methods by which it may be attempted. The first consists in estimating the thermogenesis from what is known as to the quantity and "heat value" of the material daily and hourly consumed in the body, under the conditions to be investigated; the second, in directly measuring the quantity of heat daily or hourly discharged from the body, this quantity being, if the temperature is constant, identical with the quantity produced. In employing the first plan, that of estimation, we depend entirely on certain experiments made about eight years ago at the Royal Institution, by Prof. Frankland, (the accuracy of which has been generally admitted,) by which the "heat value" of the "immediate principles" of food, (albumin fat and some

carbonic hydrates,) *i.e.*, the quantity of heat yielded by each in complete or partial oxidation, was estimated.

Of the values obtained, the most important and the most frequently used are those relating to albumin and its product urea, and to fat. A gramme of albumin, according to Frankland, yields 4·998 kilogramme-units of heat in complete combustion, *i.e.* 4·998 times as much heat as is required to raise a kilogramme of water one degree of temperature. A gramme of urea yields 2·206 kilogramme-units; a gramme of fat 9·069 k.-units. In the disintegration of albumin in the living body, it does not yield the ultimate products (water, ammonia, and carbonic acid) but nearly the whole of its nitrogen passes out in the form of urea. Consequently in estimating the quantity of heat generated by it in the organism, (its "physiological heat value,") we deduct from its total heat value, the heat value of the weight of urea which is derived from it. Now, each gramme of albumin yields one third of a gramme of urea, that being the quantity which would be produced by it if all its nitrogen were, in passing out of the body, to enter into the constitution of urea, for whereas albumin contains 15·5 per cent. of nitrogen, urea contains 46·66 per cent., and $\frac{15{\cdot}5}{46{\cdot}66} = \frac{1}{3}$. Hence of the total heat value of every gramme of albumin consumed physiologically, as much as belongs to one third of a gramme of urea, (*i.e.*, $\frac{2{\cdot}206}{3} = 0{\cdot}735$ k.-units) is lost to the organism. Deducting this from 4·998, we have 4·263 as the "physiological heat value" of albumin.

Leyden found, as has been already seen, that his fever patients exhaled during the remission, *i.e.*, when free from fever, 83·8 litres (at 0° C and 760 m.m.) of air in 15 minutes, which contained 3·3 per cent., *i.e.*, 2·79 litres of carbonic acid. A litre of carbonic acid weighs 1·9712 gramme. Consequently the discharge of carbonic acid per 15 minutes was 5·5 grammes or 22 grammes per hour. This gives 528 grammes as the discharge per day. In fever the same patients exhaled 134·6 litres in 15 minutes, containing 3·066 per cent. of carbonic acid, or, 4·127 litres. This gives 32·5 grammes per hour, or 780 grammes in 24 hours, supposing the rate of discharge to be constant. Senator, from determinations made in cases strictly comparable with those of Leyden, estimated the daily discharge of urea in patients on fever diet, but free from fever, as 17·5 grammes. We may therefore take 17·5 grammes of urea, (representing 52·5 grammes of albumin,) and 528 grammes of carbonic acid as an approximation as near as can be attained to the true estimate of the discharge of a healthy male person on fever diet.

On these data we may proceed as follows:—The physiological heat value of 52·5 grammes of albumin is 229·0 k.-units. The 52·5 grammes contain 27·82 grammes (53 per cent.) of carbon of which 3·5 take the form of urea in order to leave the organism, (for urea contains one fifth of its weight of carbon, and 17·5 grammes are discharged.) Deducting the remainder of carbon (*i.e.*, the quantity not so discharged) from 144 grammes, (the quantity of carbon contained in 528 grammes of carbonic acid,) we have 119·68 grammes as the quantity of carbon to be accounted for as derived from other sources. Now in inanition or on fever diet there is but one non-nitrogenous source of carbonic acid which we have to consider, namely, the fat of the tissues, consequently it is from fat that the 119·7 grammes of carbon must be derived. Taking the per-centage of carbon in fat as 76·5, we have 156·4 grammes as the weight of fat, which must have been consumed in order to produce the quantity of carbonic acid actually discharged. According to Frankland's estimate 156·4 grammes of fat yield in disintegration 1419 k.-units of heat. Adding this to the quantities derived from the disintegration of albumin we have 1648 k.-units as the total quantity of heat produced by patients on fever diet but in the apyretic state.

By substituting for the numbers given above relating to the discharges

in health, those relating to fever and repeating the process, we arrive at a comparable result as to the febrile production of heat. In fever, according to Senator's estimate, the urea discharge is increased to about 40 grammes daily, *i.e.*, it is about two and a third times as great as it would be on the same diet in health. Leyden's estimate of the carbonic acid discharge has already been given as 780 grammes daily. The physiological heat value of 120 grammes of albumin (the quantity which corresponds to 40 grammes of urea) is 511·56 heat units. The 120 grammes contain 63·6 grammes of carbon, of which 8 grammes leave the organism in the form of urea. The remainder of carbon (55·6 grammes) having been deducted from 212·7 grammes, the total carbon-discharge by respiration (*i.e.*, the quantity of carbon corresponding to 780 grammes of carbonic acid) we have 157·1 grammes as the weight of carbon to be accounted for by the consumption of fat in the body. The weight of fat required for this purpose is 205·3 grammes, which would yield 1862·4 k.-units. Adding this, as before, to the quantity of heat derived from the disintegration of albumin, we have 2373·9 as the total heat production of fever.

Ranke found in his experiments on himself that on an adequate mixed diet, *i.e.*, on a diet sufficient, and not more than sufficient, to maintain nutritive equilibrium, he discharged in twenty-four hours a quantity of nitrogen corresponding to 32·3 grammes of urea, and that his respiratory discharge of carbonic acid was 791 grammes. Proceeding as before we have 413·5 k.-units as the quantity of heat yielded by the disintegration of 97 grammes of albumin, which in this case was of course derived from food. Of the carbon contained in this 97 grammes, 45 grammes would have to be discharged in carbonic acid. Deducting these from the total discharge of carbon, viz. 215·7 grammes, we have 170·7 grammes of carbon, to be accounted for as derived from the non-nitrogenous constituents of food. The diet consisted of 250 grammes of meat, (containing a very small proportion of fat,) 400 grammes of bread, 70 grammes of farinaceous food, 70 grammes of egg-albumen, and 100 grammes of butter and lard. From previous determinations it was estimated that the fat of the meat contained about 2·8 grammes of carbon, the butter and lard about 67·9 grammes, the farinaceous food about 26 grammes. This leaves 74 grammes to be accounted for as having been derived from the bread, for 2·8 + 67·9 + 26 + 74 = 170·7. 170·7 grammes therefore represents the balance of carbon in the expired carbonic acid, not already accounted for as derived from the disintegration of albumin. (The actual quantity of carbon contained in the carbonic hydrates of the bread was 80 grammes, so that we have an excess of 6 grammes unaccounted for.) According to Frankland's table the fat would yield 33·19 k.-units, the butter 852·7 k.-units, the bread and other farinaceous food, (supposing them to contain 156·5 grammes of starch of which the heat value is 5·232,) 819 k.-units. Adding these to the 413·5 k.-units derived from the disintegration of albumin we have 33·19 + 852·7 + 819 + 413·5 = 2118·39 k.-units as the heat production of a healthy adult on a mixed adequate diet. On similar data derived from other experiments on himself, Ranke estimated his own mean heat production on adequate diet at 2,200 k.-units.

Thus we have for the three conditions we have been considering, namely, inadequate or fever diet without fever, inadequate diet with fever, and adequate diet in health, the following results:—

Inanition - - -	1648·0 k.-units
Fever - - -	2373·9 k.-units
Health - - -	2118·4 k.-units

The general result to which the preceding calculation leads us, is a very important one, namely that, although as compared with the heat-production of an individual on fever diet, the heat production of a fevered person is excessive, it is not by any means greater than the heat production of health, for the highest difference indicated by the numbers stated is, as we shall see immediately, insignificant.

In estimating the value of this result, there are several considerations to which it is requisite to call attention. In the first place, it is to be noticed that the data employed as representing respectively the discharges of nitrogen and of carbon in fever, are the highest that could be taken; thus, those relating to urea were founded on observations of fevers of short duration, and referred to periods during which the characters of the febrile state showed themselves in their fullest intensity. It is still more important to remember that the estimate of the febrile discharge of carbonic acid in 24 hours, is founded on determinations relating to the rate of discharge during the day only. In comparing the results with those relating to the same patients when free from fever, this error was got rid of, for both sets of observations were made in exactly the same way. Consequently the numbers given above, representing the relation between heat-production on fever diet without fever, and on the same diet in the febrile state, may be regarded as accurate; but if we compare either of these numbers with that representing the heat-production of health with adequate diet, a correction is required.

Taken absolutely, both of them are unquestionably too high, for it is well known that the rate of carbonic acid discharge is considerably higher in the day than in the night, so that any estimate of the total discharge from measurements made only during the day is certain to be excessive. Pettenkofer and Voit found that in health the mean discharge during the whole 24 hours falls short of the mean rate during the day by 14 per cent. If we make a deduction of 14 per cent. from the estimated febrile discharge of carbonic acid which was taken as the basis of our estimate given above, of the heat production in fever, we have to take off 109 grammes from our total of 780 grammes. Now the heat discharge corresponding to each gramme of carbonic acid derived from the consumption of fat is 3·23 k.-units; consequently if in fever the difference between day and night is as great as in health, we must take off 352 ($=3{\cdot}23 \times 109$) k.-units from our estimate. Thus corrected the numbers stand thus:—

Heat production in fever on fever diet -	2021 k.-units.
Heat production in health on adequate diet	2118 k.-units.

It is further to be borne in mind that the state of things which is understood by the term "adequate diet" is not that of ordinary life. By adequate diet is meant a diet which is just sufficient to maintain nutritive equilibrium, *i.e.*, to balance expenditure by income. Under ordinary circumstances we consume a great deal more food than is required for this purpose. In Professor Ranke's experiment, the diet of a young man of 24 consisted as we have seen of half a pound of meat, and a pound of bread, besides small quantities of butter and eggs, &c., an amount of aliment which, although it was proved experimentally to be "adequate" would, in ordinary language be described as insufficient, and is certainly very inconsiderable as compared with the usual requirements of persons of the same age and sex. From the results of his experiment on more abundant dietaries Ranke inferred that the activity of the thermogenetic processes of his body could be increased to as much

as 2,700 k.-units per diem, an amount far exceeding the highest estimate that could be made of the possible production of heat in fever.

Up to the present time no one has attempted to determine the quantity of heat produced in the human body by direct calorimetrical measurement. The only approach to such measurement is to be found in the clinical observations of Prof. Leyden as to the relative quantity of heat given off by the skin in fevers and in health, of which an account will be given in the next section; but in the dog, as has been already stated, the total heat production has been made the subject of an elaborate investigation, extending over many years, by Dr. Senator. As these measurements are the only ones which have as yet been made of this function in the higher animals, it will be necessary to give the reader a sufficiently complete account of them to enable him to understand their bearing.

In Dr. Senator's, as in all other methods of physiological calorimetry the quantity of heat given off by an animal in a given time is ascertained by measuring the loss of heat at its surface; and this measurement is effected by placing it in a ventilated chamber of which the wall is hollow and contains water.

The calorimeter consists essentially of two copper boxes, an internal and an external, resembling each other in form. The internal serves for the reception of the animal, and is provided with a cover which closes air-tight; the external contains the water, to which heat is to be communicated from the body of the animal. The inner case is suspended in the water in such a way that it is in contact with water on all sides, so that the animal occupies an air cavity which is completely surrounded by water. This cavity communicates with the external air by two ventilating channels, one for the entrance, the other for the discharge of air. The temperature of the inner box is measured by two thermometers, its contents being thoroughly agitated before the measurement. The whole apparatus is contained in a wooden case, between which and the external surface of the water-box there is a packing of non-conducting material, in order to diminish as much as possible the loss of heat. As a preliminary step, this loss was determined in a number of experiments in which the difference between the temperature of the water contained in the chamber and that of the environment varied as much as possible. From these a series of corrections for "temperature difference" were obtained. In all the experiments the chamber contained the same quantity of water, 37 litres. From the weight and specific heat of the metal contained in the boxes their calorimetrical value was estimated as equivalent to that of 2·5 litres of water, so that the total water-value of the apparatus was 39·5 litres. The term "coefficient of cooling" is used by Senator to indicate the number of kilogramme-heat-units lost by the apparatus in one hour for any given number of degrees of "temperature-difference." This was learnt by multiplying the correction for difference, by 39·5. The quantity of heat in k.-units lost by the air passing through the apparatus was of course obtained by multiplying its estimated weight by the specific heat of air (0·237) and the increase of temperature, (*i.e.*, the difference of temperature between the air entering and that passing out of the apparatus.) The ventilation was effected by a Bunsen's water-air-pump and measured by a gas meter; from this measurement the weight was estimated, the proper corrections for pressure and temperature having been made. The methods by which the carbonic acid and water were determined have been already described. From the hourly discharge of water the quantity of heat lost by evaporation was estimated.

In calorimetrical, as in all other quantitative measurements of the products

of life, it is necessary that for each result two experiments should be made, of which one is the exact counterpart of the other, with the exception that in the former the condition to be investigated is present, in the latter absent. All Dr. Senator's observations were made on this principle, that is, each measurement of the febrile heat production of an animal was compared, not with an estimated normal, representing the mean results of a number of similar experiments on other animals, but from an experiment made previously on the same animal under exactly similar conditions, fever excepted. Considering however, how important it is that a normal standard for future use in pathological inquiries should be obtained, he has recently made a series of determinations on a sufficient number of healthy animals, with this object in view. I subjoin a summary of one of these observations, which may serve as an example of the method employed in the whole research.

A dog, weighing 4,270 grm., which had been kept for four weeks on a diet of 250 grammes of selected horseflesh, with five grammes of lard, and 100 cubic centimeters of water, was introduced into the calorimetrical chamber at 9.34 a.m. The temperature of the animal when introduced was 39°·0 C., and that of the water of the calorimeter 27°·35. It remained in the chamber for four hours, during which the temperatures of the calorimetrical water, of the air on entering and leaving, and of the surrounding air, were observed every 10 minutes. The results of each hour were reckoned separately as follows: the calorimetrical value of the calorimeter, (*i.e.*, the quantity of heat required to augment its temperature by one degree,) being 3·94 k.-units and the increase of temperature during the hour being 0°·02 C., the heat communicated to it by the animal was 0·79 k.-units. Secondly, 144 litres of air having passed through it, of which the temperature was raised by 4°·48, the heat communicated to it, (= the product of the weight of 144 litres at the temperature at which it entered, the specific heat of air, viz., 0·237, and the increment of temperature,) was computed as 0·18 k.-units. Thirdly, the air on entering the calorimeter being dry, and having taken up from the animal 0·75 gramme moisture, this quantity, multiplied by 0·582, gave 0·44 k.-units.* Lastly, the quantity of heat given off by the apparatus to external media as previously determined empirically, for the difference of temperature between the temperature of the calorimetrical water and that of the external air was 11·22. Hence the total quantity of heat given off by the animal to its surroundings during the hour (= 0·79 + 0·18 + 0·44 + 11·22) was 12·63 k.-units. Similarly estimated, the discharges of heat in k.-units for the second, third, and fourth hours were severally 12·26, 11·54, and 11·92. From 26 similar measurements of six healthy animals, the following results were obtained in k.-units as representing the heat production of the dog per kilogramme of body weight, viz., 2·34, 2·71, 2·24, 2·88, 2·18, 2·85, giving a mean of 2·53 k.-units as the quantity of heat produced by a dog when fasting during summer.

In experiments relating to the influence of food on heat production it was found that the same dog which in the fasting state yielded 23·28 k.-units of heat per hour, and 5·2 to 5·5 grammes of carbonic acid, produced six hours after feeding 35·43 k.-units and 9·5 grammes of carbonic acid, its temperature remaining the same throughout. In this, as in other observations, the food given was the daily ration of flesh and fat which was sufficient to maintain nutritive equilibrium.

Production of heat in induced fever.

We are now in a position to proceed with the examination of Senator's results as to the production of heat in the fevered organism of the dog. With this view, comparative observations were made on the same animals in respect of which those relating to the discharge of carbonic acid and urea have already been given (p. 4); the measurement of heat production and of carbonic acid discharge being carried out simultaneously, that is, during periods of observation of which each lasted an hour. As was before explained, the normal heat production of each

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With reference to the determination of the heat loss by evaporation the method employed will probably be found to be open to objections, the discussion of which must for the present be reserved.

animal was first ascertained by measuring it on two successive days of privation of food. The observations were then repeated after the animal had been brought back again to nutritive equilibrium, under conditions which differed only in one respect from those of the first, namely, in the previous induction of the febrile state by the injection of fresh pus.

The following is a tabular summary of the results stated in the same form as in Table I.

Table II.

Table showing the Quantity of Heat produced per Hour by Fevered Dogs as compared with the Quantity by the same Animals when free from Fever but under the same Conditions of Nourishment.

—		Bodily Temperature (in rectum). Means	Heat Production.
Observation 1.			
Weight of animal 11 lbs. 10 oz.			
1st day	Normal	39·0	13·32
	Fever	39·3	12·46
2nd day	Normal	39·0	11·50
	Fever	40·3	11·58
Observation 2.			
Weight 13 lbs. 4 oz.			
1st day	Normal	39·1	15·67
	Fever	39·4	15·29
2nd day	Normal	39·1	17·32
	Fever	40·3	15·57
Observation 3.			
Weight 16 lbs.			
1st day	Normal	39·0	12·64
	Fever	39·6	9·91
2nd day	Normal	38·8	11·87
	Fever	40·7	14·52
3rd day	Fever	40·7	11·87
Observation 4.			
Weight 10 lbs. 10 oz.			
1st day	Normal	39·3	8·67
	Fever	39·5	9·59
2nd day	Normal	39·3	10·24
	Fever	40·7	11·86
3rd day	Fever	39·6	9·43
Observation 5.			
Weight 9 lbs. 2 oz.			
1st day	Normal	38·9	12·31
	Fever	39·7–40·3	11·97
2nd day	Normal	38·9	12·67
	Fever	41·0	15·22
Observation 6.			
Weight 24 lbs.			
1st day	Normal	39·0	24·18
	Fever	39·2	25·46
2nd day	Normal	39·0	24·48
	Fever	40·0	23·59

		Morning.	Afternoon.	Morning.	Afternoon.
Observation 7.					
Weight 12 lbs. 9 oz.					
1st day	Normal	38·8	38·8	15·94	16·20
	Fever	38·7	40·7	15·34	17·44
2nd day	Normal	38·8	38·6	16·47	17·06
	Fever	40·0	40·0	15·48	19·50
3rd day	Fever	40·4	39·9	17·41	15·57

A glance at the above results is sufficient to show that they afford no ground for concluding that in the induced fever of the dog there is on the whole any increase of heat production. One or two instances no doubt, as for example the observations relating to the second day of fever in the first series, and to the third day in the third and seventh series, might be referred to in favour of increased production; for in these cases the discharge of heat was increased, at the same time that the temperature of the animal rose. But in others, as in those relating to the second day in series 2, 6, and 7, although the temperature in each instance remained unaltered, the calorimetrical result was decidedly less than normal.

In series 7, the observations were more complete than in any of the others. The period during which the heat production and the discharge of carbonic acid was measured was extended to four hours, of which three were consecutive (10 a.m. to 1 p.m.), and the fourth separated by a four-hours' interval (5 to 6 p.m.). The "insensible loss" was also determined for each day of observation. The insensible loss was increased more than 50 per cent., it being 85 and 75 grammes respectively on the first and second normal days, and 142 and 151 grammes during the corresponding days of fever. All of this increased loss of weight must have been due to increased discharge of water, for the determinations of carbonic acid for the same days show that the rate of discharge of this product was rather diminished than increased. Notwithstanding this fact, the weight of aqueous vapour taken up during each hour of observation by the air transmitted through the chamber, was not greater in the fever series than in the others. As, however, in all the observations the total quantity of aqueous vapour discharged by this channel (two or three grammes) is shown by the detailed results of the experiments to have been small as compared with the very considerable "insensible loss" per hour, the discrepancy may perhaps be attributed to the insufficiency of the ventilation employed (about 150 litres per hour).

Dr. Senator concludes his discussion of his calorimetrical results as follows:—

In the first stage of fever the discharge of heat is rather diminished than increased, so that at this period it is probable that there is an abnormal retention. As the febrile process progresses, and when it is at its height, fluctuations exhibit themselves in the quantity of heat liberated, which resemble those which are observed in the discharge of carbonic acid and of aqueous vapour; but it cannot as yet be determined whether the amount of heat given off during the whole course of the febrile process is greater or less than the quantity of heat given off during the same period of apyrexia.

In judging of the significance of the fact last stated, it must be borne in mind that the normal with which the febrile thermogenesis is here compared, is that of inanition. In the dog, when on adequate diet, the production of heat is at least 50 per cent. more active. If, therefore, we were to take the animal in the ordinary condition of nourishment as our standard of comparison, we should find the heat production in fever very considerably diminished.

Section 2.—Clinical Investigations of the Discharge of Heat from the Skin.

It has been seen in the last section that in the fevered animal, in respect of which the conditions are such as to admit of exactitude of measurement, such measurement affords no support to the hypothesis

that increased thermogenesis is a characteristic of the febrile state. In man no attempt has yet been made to measure the heat production of the whole body. It has, however, been concluded from the results of observations as to the emission of heat from the cutaneous surface in those fevers which come under clinical observation, that the production of heat in the whole body is augmented. Here, again, as with regard to the discharge of carbonic acid, the pathologist depends almost entirely on the observations of Professor Leyden.

The series of researches to which we have now to refer were made in 1868.* They were directed exclusively to the relation between pyrexia, loss of weight, and discharge of heat from the surface in fever, the subjects of observation being for the most part persons affected with relapsing fever, typhoid fever, or pneumonia.

For the investigation of the surface loss of heat, a water calorimeter was employed, which was constructed on the same principle as that already described as applicable for the investigation of the discharge of heat in animals, with the exception that there was no provision for the continuous passage through it of a current of air. The apparatus is of such form and dimensions as to contain one limb instead of the whole body.

The copper chamber in which the limb is contained during the observation is 2 feet long and 1 foot wide. It is surrounded by a cylinder of zinc of corresponding form, but from 3 to 4 inches wide. The outer wall of the water chamber is protected from abstraction of heat by a thick padding of non-conducting material enclosed in a wooden case. The equal distribution of heat in the water contained in the chamber is secured by two agitators, turned by a winch, which revolve round the outer surface of the cylinder, so as to maintain a continuous current in the direction of rotation. The open end of the chamber is lined by an annular air cushion of india rubber, which, when the limb is introduced, occupies the space between its surface and that of the copper, so as to close the chamber air tight. The part of the body observed is the leg, the lower extremity being introduced into the chamber to such a distance that the india rubber cushion gently presses round the knee immediately above the joint.

Each observation lasted two hours. Before beginning it the water in the calorimeter was brought to the temperature of the room, the variations of which were of course noted. The greatest pains were taken that the limb, as placed in the chamber, should be under otherwise normal conditions, and particularly that it should be carefully supported on a kind of wooden tray contained in the chamber, so as to avoid contact with the metal, and that it should be clothed with blanket of the same thickness as the leg of the opposite side. When these precautions were attended to, it was found not only that its introduction into the calorimeter did not at all interfere with the comfort of the patient, but that the conditions and temperature of the limb were at the end of the two hours the same as those of its fellow.

The mode of estimating the results of the observations was as follows :—According to Funke † the surface of a grown person is 2,254 square inches, that of the leg alone 149 square inches, the two numbers being in the ratio of 15 : 1. The calorimetrical value of the chamber is 55 k.-units. The mean rise of temperature produced in an hour by

* Leyden. Untersuchungen über das Fieber. Deutsches Archiv Vol. V. pp. 273–371.

† Quoted by Leyden. I am not able to ascertain in what paper of Funke's these facts are recorded.

the introduction of the limb of a healthy person was 0°12 C. Hence 6·6 k.-units (55×0·12) must have been given off to it by the limb in one hour. Assuming that the quantity given off was in the same proportion to its surface, we have 99 k.-units as the hourly heat discharge, *i.e.*, production of the body. This corresponds pretty closely with the estimate already given of the normal heat discharge in health, viz., 2,200 to 2,600 k.-units; for 24×99=2,376. This is probably high; for if we add to it the 400 k.-units which, according to Helmholtz's estimate are given off by the lungs, we have a total of more than 2,700 k.-units for the total heat loss.

The following is a tabular summary of the most complete of the series of observations reported in Professor Leyden's paper. It relates to two cases of relapsing fever and two of pneumonia. The table scarcely requires explanation. In the first case the observations were made during the accession, during the first remission, and the following relapse; in the second case the observations were begun during the first remission and continued during the second relapse and the second remission. In the table each line gives the result of an observation; the patient's temperature and pulse are stated in columns 4 and 5, while column 6 shows the rise of temperature produced in the calorimetrical water in the course of one hour. As has already been stated it was found that in a healthy person the mean rise of temperature produced in the course of one hour was 0°·12 C. when the ward was at the ordinary temperature, viz., 17°·3 C. (63°1 F.).

Table Showing the Results of Observations relating to the Discharge of Heat from the Surface of the Skin in Fever.

1. No.	2. Date.	3. Temperature of ward.	4. Temperature of patient.	5. Pulse.	6. Increment of temperature.	Remarks.
						Case I.—Relapsing Fever.
1	Oct. 19	18·8	40·0	120	0·19	M. æt.? Weight, 96 lbs.
2	„ 29	18·1	40·5	124	0·14	The periods of observations 2 and 3
3	„ 29	18·1	?	?	0·18	followed at an interval of half an
4	„ 30	18·5	40·3	124	0·15	hour during which a rigor occurred.
5	„ 31	19·7	41·4	120	0·13	State of skin not noted.
6	„ 31	19·8	39·5	not stated	0·20	Observations 5 and 6 were made during the relapse at 12h. 15m. and 1h. 45m.
7	„ 31	19·9	36·1	80	0·06	of the same day. Before observa-
8	Nov. 8	17·5	37·3	80	0·105	tion 5 the patient had had a rigor, and the skin was hot and dry. At 1h. 15m. sweating came on, which continued during the period of observation. Observation 7 was made at 5h. 35m. the same day; observation 8 at mid-day when convalescence was established.
						Case II.—Relapsing Fever.
1	Nov. 14	20·5 mean	39·8	108	0·16	M. æt. 18, weight 101 lbs.
			38·7	88	0·19	The numbers bracketed relate to a
			—	—	0·24	period of observation of 5 hours,
			37·2	64	0·16	during which the bodily temperature
			37·2	—	0·15	was gradually sinking. The patient

1. No.	2. Date.	3. 4. Temperature of ward.	Temperature of patient.	5. Pulse.	6. Increment of temperature.	Remarks.
2	„ 15	20·5	36·8	64	0·075	was sweating the whole time, most profusely during the middle hour, when, as seen in column 6, the surface loss of heat was greatest.
3	„ 16	20·3	36·5	68	0·10	
4	„ 17	20·5	36·5	64	0·06	
5	„ 18	20·0	36·5	68	0·10	
6	„ 19	20·0	36·5	68	0·10	Observations 2 to 6 were made on different days during the non-febrile interval. Each observation lasted two hours, of which the mean result is given in each case. The patient was perfectly free from fever.
7	„ 20	19·6	40·6	106	0·145	
8	„ 21	19·4	40·4	108	0·145	
9	„ 22	19·4	39·0 to 40·7	110 to 104	0·142	
10	„ 23	—	40·5	not stated	0·10	Observations 7 and 8 were made at 11 a.m. and 6 p.m. of the first day of the relapse. The skin was dry and hot, moaning constant, excessive thirst. In the afternoon the temperature rose to 41°·0.
11						Observation 9 was continued for four hours, viz., from noon to 4 p.m. During the whole time the skin was hot and dry.
12	„ 23	19·5	38·9	104	0·20	Observation 10 lasted two hours, commencing at 11 a.m. The skin was hot and dry. Observation 11 lasted also two hours, commencing at 5h. 45m. p.m. In the course of it the patient began to sweat, and continued to do so all the evening. At 8h. 15m. observation 12 was taken.
	„ 23	—	37·4	88	0·18	
						Case III.—Pneumonia.
1	Jan. 8	18·8	40·0	100	0·192	M. æt. 19. Weight 101 lbs.
2	„ 8	18·8	39·2 to 37·2	92 to 76	0·26	Observation 1 was made at mid-day, the skin being moist. Observation 2 at 6h. 30m. p.m., the perspiration being general over the whole body.
	„ 11	18·6	37·1	not stated	0·105	Observation 3 relates to convalescence.
						Case IV.—Pneunomia.
1	Jan. 11	19·5	39·7 to 40·5	100 —	0·14	M. æt. 30. Weight 130 lbs.
2	„ 12	19·9	40·3	100	0·175	
3	„ 13	19·5	39·3 to 38·4	100 —	0·225	
4	„ 14	19·5	40·2	108	0·23	
5	„ 20	17·0	Normal.	Normal.	0·11	

Before proceeding to examine the results contained in this table, it will be advantageous to state the signification attached to them by the author, and accepted by other authorities on the pathology of fever. Dr. Leyden expresses his conclusions as follows:—"The discharge of

" heat is increased in fever whether the temperature is constant, falls " or rises. Consequently it is certain that the production of heat is " increased. In high fever the quantity of heat given off is from half " as much again as the normal to twice as much. The most rapid " discharge of heat takes place in the critical stage when the tem- " perature is rapidly sinking. It may then be twice or even three " times as great as the normal. Defervescence is associated with " marked sweating and evaporation at the surface; fervescence by the " absence of these phenomena, even when the coverings are air tight."

Senator's conclusion on thermogenesis.

In dealing with the question we have now before us, Senator, in the paper already so often quoted, seeks in Leyden's researches the most important material for the construction of his doctrine of pyrexia. In beginning his chapter on this subject he says:—" By Leyden's observations these two facts " come out prominently. 1. That with the exception of the initial stage, the " discharge of heat is considerably increased, although by no means constantly. " 2. That the activity of the discharge is not proportional to the bodily tem- " perature, for it may be less when the temperature is high, than when it is " lower; it may be normal when the temperature is above the normal, always " attaining its maximum in the stage of defervescence with critical sweating," &c. He then after referring to the confirmatory results of Liebermeister and Hattwich, and giving an explanation of the apparent contradictions between Leyden's general conclusion that in fever the production of heat is nearly doubled, and the contrary results obtained by himself in his calorimetrical measurements of fevered dogs, proceeds to observe that notwithstanding that the observations of Leyden extended at the utmost over a few hours, and related only to the discharge of a part of the body, it appears to him to be permissible to found conclusions upon them, so long as it is understood that they are accepted subject to drawbacks, which may turn out to be more important than they at first sight seem. " We may therefore," he says, " estimate the average increase of heat loss in febrile pyrexia as compared " with the normal as 70–75 per cent. As, moreover, at this time the constant " temperature of the body is higher, it must have at its disposal in pyrexia an " even larger quantity of heat than is required in the non-febrile state to " maintain itself at fever temperature; a quantity which not only exceeds " that produced by a healthy person in inanition or on fever diet, but even that " generated in ordinary conditions of nourishment. In making this estimate " it must, however, be expressly stated that it applies only to the condition of " fervescence, and that it must not be taken as representing the total loss of " heat in the process, from the beginning to the end; for during the defer- " vescence the loss is much greater, and it is much less during the accession." Senator's general conclusion on the subject is stated as follows:—" The discharge " of heat is in the outset of fever during the rigor, not increased but " diminished; during the height of the fever it is on the whole increased in " the ratio (so far as relates to the day hours) of 70–75 per cent., and con- " siderably more during the critical defervescence. During the height the " greater part of the loss occurs by conduction and radiation, during the " crisis by evaporation."

Results corroborative of those of Leyden are furnished by the observations of Liebermeister as to the quantity of heat given off by a fever patient in the tepid bath, as compared with a healthy person. Regarded as calorimetrical experiments, these measurements are subject to objections which cannot now be considered.

I have quoted these passages in order to show that Senator and Leyden, the two greatest authorities on the pathology of fever, are agreed in accepting the fact as certain that production of heat is largely increased, and that both of them found their conclusions simply and exclusively on Leyden's cases, for although both of them refer to Liebermeister's observations in confirmation, each indicates some of the reasons for regarding the results of that observer as inapplicable to the question.

If, therefore, it can be shown that Leyden's facts admit of a different interpretation, the whole foundation of the very generally accepted belief that the heat production is greater in fever than in health under normal circumstances of nutrition, falls to the ground.

Statement of the question.

The question we have before us is not whether the fact that in febrile pyrexia the temperature is as a rule increased both in man and animals by two or three degrees, is due to this or that cause, but simply whether in fever along with the increased temperature, there is also increased production.

That *cæteris paribus* there is, in fever, an increased activity of *certain processes* which produce heat can be proved without calorimetrical measurement. Supposing the state of the heat discharging surfaces to remain the same, the fever patient must necessarily produce more heat to keep his body up to the higher mark as regards temperature than the healthy person. In other words, supposing the quantity and quality of clothing, and the temperature and moisture of the air to remain the same, and the discharge of watery liquid from the sweat glands to be also the same, the fevered person would give off a somewhat larger quantity of heat from the surface than a healthy person; for the difference between the temperature of his body and that of the environment being greater, the loss by radiation and convection would be proportionally greater. The difference, however, would certainly be small, greater somewhat in summer than in winter, and greater in bed than in clothing.

It is also certain that the process of disintegration of tissue of which the evidence has already been presented to us, is in its nature thermogenetic. In the preceding section I have estimated that increase, and have shown that there is unquestionably a very considerable difference between the heat production of a febrile and of a non-febrile person on the same febrile diet. I have also pointed out that this holds true only so long as the comparison is made under similar conditions of nutrition, for if we compare the heat production of a fevered patient with that of a person in health on ordinary diet, we find that whatever difference presents itself is quite within the limits of normal variation.

The fact of the greater consumption of material in fever may therefore be dismissed entirely from our minds in entering on the consideration of observations similar to those of Professor Leyden, for in those observations the comparison between fever and health is made, not in regard of the discharge of heat from the whole body (pulmonary and cutaneous), but in regard of the quantity of heat liberated by a given area of skin, in fever and in health. Whatever may be the result of a comparison between these two conditions as regards the activity of the process by which heat is given off by the skin, there is no reason for supposing that a well-fed person would, if the skin were in a natural state, emit more heat from a square inch of surface than an ill-fed, or that the quantity of heat given off by the skin is dependent on any other cause than on changes in its own temperature or moisture, or in that of the atmosphere with which it is in contact.

The careful study of Professor Leyden's results has led me to an interpretation which differs materially from that which he has embodied in his main conclusion. He admits throughout the great importance of visible perspiration, *i.e.*, of the secretion of watery liquid by the sweat glands as a condition favouring the discharge of heat from the skin. He points out that in all those of his experiments in which the heating of the calorimetrical water was most rapid, the result could be connected with rapid cooling of the accessible parts of the body, and with profuse sweating. But he finds that there were other cases in which, notwithstanding the dryness of the skin, the fevered body parted with its heat to the calorimeter with a rapidity which could not possibly be accounted for as the mere result of the greater heat of the surface. In looking through the cases, I am unable to find a single instance in which the

state of the skin being noted, it was found that in the absence of perspiration, the loss from the surface was considerably in excess. This being so, I am compelled to associate increased discharge from the surface, not with pyrexia, but with sweating, for while on the one hand I find instances in which the patient was in high fever, with only an average of heat loss, I find in the same patient on another day a very active discharge of heat from the surface, but no fever.

In so far as it can be shown that the increased rate at which the fever patient's heat was communicated from the limb to the calorimeter in which it was enclosed, is dependent on sweating, the result is of little value or significance as an index of increased production of heat in the living tissues. Under the conditions of the experiment, *i.e.*, when a limb is enclosed in an air-tight chamber, the air which occupies the space between the cutaneous surface and that of the chamber, soon becomes saturated with moisture. As soon as this state of things is established there is no further loss of heat by the conversion of sweat into vapour; the effect of sweating therefore resolves itself into the mere abstraction from the limb of a certain quantity of watery liquid, of which the whole of the heat goes to the good of the calorimeter. So far as the body of the patient is concerned, the process is attended with the loss of a certain quantity of water, and manifests itself in a corresponding loss of weight, but so far as relates to the chemical processes by which heat is produced, it fails to afford any information. If for every gramme of water sweated out at the surface, it were the law of the animal economy that an equal quantity of cold water should be ingested, then it might be said with truth that for every gramme discharged a quantity of heat must be generated in the body sufficient to warm a gramme of water from the ordinary temperature to that of the blood. So far from this being the case, the loss of water is, as a rule, supplied in the diet of fever by liquid, of which the temperature is as high as, or higher than that which it has to acquire in order to be discharged, in which case it is obvious that the water as it actually leaves the body cooler than it entered it, must, (in so far as it has any appreciable action on the temperature of the body,) tend rather to favour the accumulation of heat than to promote its discharge.

Professor Leyden's observations are of great value, as affording a more complete understanding than we before possessed of the function of the sweat glands in defervescence. In this respect some of the observations (as *e.g.* the second case in the table) are particularly striking. In that instance, as in many others, it was seen that the temperature of the patient's body sank very rapidly as that of the calorimeter rose, the transference of heat from one to the other being effected either by the trickling down of drops of hot moisture from the limb on to the floor of the chamber, or through the air by a process of distillation, in which for every quantity of water condensed on the metal surface a similar quantity is evaporated from the skin. In those parts of the surface which are not enclosed in a chamber, it is clear that the sweating must be more effectual than in the chamber itself; for here the air which is in contact with the skin is not saturated, so that, in addition to the loss of heat by the discharge of warm sweat, there is an additional loss due to the conversion of the whole or part of it into aqueous vapour. In either case the activity of the process is dependent entirely on the secreting function of the sweat glands, *i.e.*, on the quantity of watery liquid which they throw out on the surface, and has no direct connexion with any heat-producing or other nutritive processes having their seats in the tissues. Whether the watery discharge is converted into vapour or soaks into the patient's

blankets, it is discharged without any arrangement existing or being required for its continuous replacement, so that, if I may be permitted to use the expression, the loss of heat by sweating is payment out of capital; it may go on for a very long period without any appreciable effect excepting loss of weight. For this very reason, of all functional fluctuations, those of sweating are the most valueless as outward indications of inward changes.

Part III.—Pyrexia.

Section 1.—*The Norma of Temperature.*

The temperature of the healthy human body has been recently determined by Jürgensen* on a larger basis of accurate measurements than before existed. The mean temperature of day and night of a healthy person, as measured in the rectum, is 37°·2 C. If the whole period of 24 hours is divided into two, of which one, commencing at the moment that the bodily temperature reaches its morning minimum, ends with the attainment of the evening maximum, the other, corresponding to the interval, it is found that in the diurnal period, viz., between 7 or 8 a.m. and 9 p.m., the mean temperature is 37°·34, while in the nocturnal period, of which the duration is shorter in the proportion 100 to 136, the mean temperature is 36°·94.

In relation to our present inquiry, Jürgensen's researches have led to a most remarkable result, which was entirely unexpected, viz., that the *mean* temperature of the human body is remarkably independent of the conditions which temporarily affect the production of heat, even when their influence is most powerful. Thus, by observations on a vigorous and healthy person who voluntarily submitted to inanition for 63 hours, it was found, not only that the mean temperature of the two days was exactly the same as in ordinary conditions of nutrition, but that the diurnal temperature course was not modified in its character.† Again, it was ascertained by the most accurate observations on the same patient, who submitted to a succession of cold baths, each lasting 25 minutes, at temperatures varying from 9° to 11° C. (50° F.) that notwithstanding the rapid abstraction of heat, which gave rise to a shivering lasting for several hours, the diminution of bodily temperature which occurred during the bath was followed, after an interval of four or five hours, by an elevation which precisely compensated it, so that if the average was taken of observations extending over a sufficiently long period, the mean was the same as under normal conditions.

An exactly similar result was come to as regards muscular work, showing that as in the former case the depression, so here the elevation of temperature by active exercise is, in the long run, completely made up for.

When it is remembered that all these conditions—inanition, abstraction of heat by the cold bath, and muscular work—are known to produce very considerable effects on the exchange of material in the body and consequently on the thermogenesis, they afford the strongest possible evidence that increased or diminished temperature has no necessary connexion with increased or diminished production of heat.

The extension of Jürgensen's observations to fever, led him to the remarkable discovery that in continued fever, and particularly in typhoid,

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* Jürgensen, Die Körperwärme des gesunden Menschen. Leipzig, 1873, p. 9.

† Jürgensen, l. c. p. 21.

the diurnal variation of bodily temperature closely resembles that of health; so that if two curves representing these variations are inscribed one above the other over the same abscissa, they are seen to run parallel to each other with a constancy which is very remarkable. In other words, the only material difference between the two conditions is that in fever, the normal is 3° higher (40°·1 to 40°·3 instead of 37°·2). Whatever be the explanation of this, the fact comes out so clearly as the result of observation, that it cannot be disputed. It affords evidence that the laws which regulate the temperature of our body, and to which even the chemical activity of our protoplasm is subject, are not upset in the febrile state, and gives us ground for anticipating that, whenever those laws shall have been fully investigated, they will be found to be the expressions of the most fundamental and specific endowments of our being.

That the shifting of the abscissa of the temperature curve three degrees upwards, does not, as Liebermeister thinks, signify that in fever the organism has "forgotten" the "habit" of temperature, is proved by the observations of the most accurate clinicists as to the influence of anti-pyretic remedies, and particularly of cold and quinine. We have already seen that in health "the law of temperature" is strong enough to withstand even the most rapid abstraction of heat from the surface; but this is not so in fever. Clinical observation has established the fact (whatever may be its therapeutical value) that in typhoid and other fevers the temperature can be brought down and kept down nearly to the normal by the systematic use of the cold bath, or of the cold affusion. Hence we are justified in concluding that in fever, conformity with the law of temperature is not abolished, but merely weakened; that just as in health a *nisus* constantly exists towards excess, which is restrained by the controlling influence of that "*schützendes Etwas*," the existence of which we unconsciously refer to when we call it the law of temperature; so in fever that influence still exists and needs only to be strengthened or aided; strengthened when we administer large doses of of quinine, aided when by the cold bath we abstract heat from the surface. It is on this principle only that we can understand how it is that those anti-pyretic agents, of which the action is so certain in fever, have no permanent effect on temperature in health.

Section 2.—Relation between Pyrexia and the other Functional Disorders of the Febrile State.

Whenever two actions or groups of phenomena are associated so as to constitute a process, the theory or explanation of that process consists in determining what is the nature of the association. And if we designate the two associated actions or phenomena respectively *a* and *b*, then the possibilities to be considered are that *a* may be the consequence of *b*, that *b* may be the consequence of *a*, or that both may stand side by side as collateral products of some other antecedent. So in the case of fever with its two chief phenomena pyrexia and textural disintegration, the theory of the process is involved in the question whether the former or the latter is primary, or whether both are not the results of an action originating independently of either.

I have referred to these questions not with a view to their immediate discussion, but for the purpose of indicating what form should be given to our investigation of the subject, in order that eventually we may find ourselves in a position to answer them.

The temperature of the body being dependent on the balance of the production and discharge of heat, of which the former is a function of

living protoplasm, the latter a function of the organs of circulation, respiration, and secretion, the question whether pyrexia or textural disintegration is primary, comes to assume the form in which it has been frequently discussed by pathological authors, viz., whether it is production or discharge which is primarily disordered.

Want of information as to the normal relation between the former of these processes and the bodily temperature, renders it impossible to answer the question in either of its forms, in other words, to frame a theory of fever. All that can be attempted is to study the mutual reactions on each other of the two sets of functional disorders, in order that when these relations have been ascertained by observation, we may be furnished with such anticipations as to their nature, as may guide us in clinical and experimental researches. With this view I shall occupy the remainder of this section, by giving an account of the agencies which exist in the animal body for regulating the discharge of heat, stating with respect to each of them what is known as to its nature; for inasmuch as we as yet *do not* know by observation or experiment of any mechanism, any endowment of living protoplasm by which it can regulate or limit its own chemical, *i.e.*, thermogenetic processes, and *do* know how the escape of heat from the surface is limited, it is clearly necessary to satisfy ourselves by the most careful observation that these agencies are inadequate, before we fall back, as I anticipate we shall eventually do, on a process having its seat in protoplasm, and seek for the explanation of the regulation of temperature in the establishment of a direct relation between it and the functional activity of living tissue.

a.—Discharge of Heat by Sweating from the Skin.

This subject has already been discussed in connexion with Leyden's researches on febrile thermogenesis. No precise measurements exist of the quantity of moisture (aqueous vapour) discharged by the human skin in health, and consequently no estimate can be formed of the heat normally lost in this way. According to Helmholtz's calorimetrical investigations the total loss of heat by the skin, amounts to about 1,800 to 2,000 kil.-units daily; Leyden's experiments have shown that this loss would be doubled in the moderate sweating of the febrile crisis, if the whole of the heat contained in the perspired water were abstracted from the organism. As has been already pointed out, this is never likely to be the case, for however well the body of a patient may be ventilated, the ventilation is never sufficient under ordinary conditions to carry away the secreted water as vapour, as fast as it is discharged by the sweat glands. If it were sufficient, the abstraction of heat from the body would be extremely rapid. We have no data for estimating it in fever, because we have no measurements of the quantity of water actually discharged. In the Turkish bath the loss of water often amounts to 500 to 600 grammes per hour. If this weight of water were entirely converted into vapour it would imply a loss of heat amounting to some 300 to 360 k.-units, which, (supposing the specific heat of the body to be nearly equal to that of water,) would cool it 6° or 7°. In fever the quantity of liquid sweated can never or very rarely be comparable to that discharged in the Turkish bath, but even here, if it were completely converted into vapour the heat loss would be very rapid.

b.—Discharge of Heat by Respiration.

The normal loss by respiration may be estimated as about 320 to 330 k.-units daily, made up of 80 to 90 k.-units, spent in warming some

10,000 litres by about 25° C. and 240 k.-units used in evaporating 412 grammes of water. This loss may obviously be increased by any cause which increases the activity of respiration.

Thus in fever, when in general the quantity of air breathed has been shown by Leyden's researches to be increased by more than 50 per cent., it is probable that other things being equal, both the evaporation loss, and that incurred in warming the air respired, will be correspondingly increased ; but, considering that the total respiration loss, according to Helmholtz, amounts to about 20 per cent., the pulmonary cooling is without doubt of little importance as compared with that which takes place by the surface of the skin.

In the dog the influence of respiration on temperature has been shown by Dr. Riegel to be much more considerable, and has an unquestionable importance as a regulating agency. In that animal any cause which elevates the bodily temperature, whether this is effected by clothing the body in non-conducting material, or placing it in a warm environment, excites respiration in a very remarkable manner, so that the animal not only breathes more frequently, but inhales a larger quantity of air at each breath. This effect, which must be attributed to the influence of the increased temperature of the blood on the intra-cranial nervous centres, was first described by Ackermann under the term heat-dyspnœa. It is not, however, so much with reference to the mode in which it is produced, or to its teleological significance that it is now referred to. Riegel* has shown that in the heat economy of the dog, the function of respiration is the most important means which exists for the maintenance of constancy of temperature. When a dog is observed in a moderately overheated room, say at 25° R. (88° F.), a temperature which to the human organism is not uncomfortably high, it soon becomes distressed and breathes with extraordinary rapidity. If under these circumstances its temperature is observed continuously, it is found scarcely to exceed the normal; but if, while still in the warm room, it is placed fully under the influence of chloroform, (a drug which under ordinary circumstances invariably decreases the temperature of the dog,) its temperature rises at once to that of pyrexia. In this experiment the reason why the temperature rises, is evidently that the narcotic renders the nervous system incapable of reacting against the stimulus to which it is exposed. Consequently the rise of the temperature of the blood is no longer the signal for that more active breathing by which, if the animal were not narcotized, the normal state of things would be restored.

c.—Influence of Changes in the Circulation on the Discharge of Heat.

The explanation which is commonly given of the nature and cause of febrile pyrexia is founded on the supposition that in health the constancy of the bodily temperature is dependent on the power which the organism possesses of regulating the circulation, that is to say, that the faculty which man in common with other homoiothermic animals enjoys of maintaining equability of temperature, depends on the existence in his nervous system of apparatus by which the relative quantity of blood contained in those parts of the vascular system which are exposed to the influence of external media, (particularly in the vessels of the lungs and skin,) can be increased or diminished according to the requirements of the organism. In constructing a theory of fever on this basis, it is

* Riegel. Ueber den Einfluss des central Nervensystems auf die thierische Wärme. Pflüger's Archiv, Vol. V., p. 651.

assumed that the disorder of the circulation is the first link in the chain of phenomena of which the febrile process consists, and consequently, that fever has its origin in disorder of the nervous system. For inasmuch as it is known experimentally that the distribution of the blood is entirely regulated by "vasomotor centres," it is clear that no departure from the normal condition of the circulation can happen otherwise, than by virtue of an antecedent disturbance of the functions of those centres.

Until a very recent period the knowledge which existed as to the influence exercised by variations of the velocity of the blood stream and of the distribution of the blood on the bodily temperature was chiefly theoretical, consisting rather of deductions from what was known as to the mechanism of the circulation than of results derived directly from observation. During the last few years a more or less complete experimental basis has been furnished by the physiological researches of Heidenhain, as well as by the pathological inquiries of Riegel and Naunyn,* so that although there are still questions which must be left open, there are some points on which it is possible to speak with confidence.

One of the most satisfactory and (if I may be permitted the expression) one of the most elegant proofs that by increasing the quantity of blood in circulation in an exposed part, the temperature of the whole body can be diminished, is afforded when the vessels of an exposed organ are paralysed by the severance of its vasomotor nerves, so that while the capacity of its relaxed blood channels is largely increased, the force of the circulation remains unimpaired. Thus, when in the well-known experiment which 20 years ago led to the discovery of the vasomotor nervous system, the vascular nerves of the rabbit's ear are divided, the increased warmth thereby produced in the ear is associated with a diminution of the temperature of the whole body, which though small in amount is perfectly measurable. It is small because the quantity of blood which is in circulation at any moment in the paralysed organ is a mere fraction of the whole mass of the contents of the vascular system.

When the vessels of the whole or of the greater part of the body are thrown into a state of relaxation by severance of the spinal cord, the resulting abnormalities of bodily temperature are much more considerable, but their nature and degree depend rather on the secondary effect which the total disappearance of arterial tonus exercises on the circulation, than on the altered distribution of the blood-current. For when all the arteries are relaxed, the velocity of the circulation, *i.e.*, the quantity of blood discharged by the heart in a given time, is necessarily diminished, the reason of this being that, while the mass of blood contained in the whole circulatory apparatus (heart and blood vessels) remains unchanged, the capacity of the vascular system is augmented, and consequently that of the heart diminished. The heart, therefore, containing a smaller quantity of blood at the commencement of each contraction, discharges less, *i.e.*, works with less effect.

Although it might have been anticipated from previously existing knowledge as to the mechanical conditions of the circulation, that this would be the case, *i. e.*, that abolition of arterial tonus would be disadvantageous to the circulation, the fact that it is so was not only not recognized, but, by many physiological writers, distinctly denied. The mechanical physiologists of the French school, whose doctrines have

* Dubczcanski und Naunyn. Beiträge zur Lehre von der fieberhaften Temperaturerhöhung. Archiv für Pathologie ; Vol. I., p. 181.

been popularized in this country by the works of M. Marey,* teach without any reservation that the effect of general relaxation of the blood vessels is to increase the force of the pulse, and to augment the frequency of the contractions of the heart, and found upon this notion their theory of fever.

d.—Comparison of the State of the Circulation in Fever with its State after Injury of the Spinal Cord.

If in man or in an animal, severance of the cord takes place below the origin of the phrenic nerves, the respiratory movements, although altered in their character by the paralysis of the muscles of the trunk, continue, and consequently, life is preserved. The phenomena which present themselves in these cases, from their extreme interest in connexion with the heat economy of the living body, have of late years concentrated upon themselves the attention of pathologists. Those which are of most importance in relation to our present inquiry are the following:—

For the reason already stated, section of the cord at the level of the seventh vertebra, or accidental destruction of the organ in man, produces as its primary effect an enormous diminution of the pressure on the arteries in consequence of which the circulation diminishes. The influence exercised by this diminution on the temperature of the body varies both in degree and direction, according to the animal observed, and the nature of its environment. In man, as is well known from the historical case recorded by Sir Benjamin Brodie, as well as from others published since, it often happens that the bodily heat rises above the normal, sometimes above that of fever. In small animals, such as rabbits, the temperature falls rapidly, notwithstanding that they are so well clothed in fur, and that the observation is made in summer weather. In animals of intermediate size, such as dogs, the result varies according to the outside temperature and the protection which is afforded against surface cooling, either by the natural covering or by artificial clothing. Thus, if the creature is invested in an envelope of non-conducting material, and kept in an ordinary room, the temperature of the blood inevitably rises to a height which often exceeds that of fever. Without clothing, especially if it be of relatively small size, its temperature rapidly sinks until it dies in collapse.

From these facts it is obvious that the most striking difference between the heat economy of the injured and that of the normal animal consists in this, that in the latter the bodily temperature is independent of external conditions, whereas in the former it is affected even by very slight changes in the environment. We have already seen to what an almost incredible extent this is true of man. Similarly, it is found that a healthy dog accustomed to the temperature of summer may be exposed to that of a winter's day without the slightest variation. After the cord is divided, the same animal must be clothed, even when in a warm room, else it cools too much; while if the room is only a very little too warm, it passes into a state of intense pyrexia. To prevent either result, depression on the one hand or collapse on the other, the surface loss has to be accurately adjusted to the thermogenesis by artificial means; for the animal has lost its powers of making any adjustment for itself.

As regards the heat economy of animals after section of the cord at

* *See* Marey's Physiol. de la Circulation, chap. xviii. p. 3,501.

the level of the sixth or seventh vertebra, there has been much dispute. Most observers have been content to assume, as a sufficient explanation in the case of depression of temperature, that the result is attributable to the paralysed condition of the cutaneous vessels and to the consequent increased discharge of heat at the surface. As regards the other cases, it has been generally taken for granted that there is a close correspondence between the condition induced by the injury and that of fever, and accordingly that there is, along with the augmented disengagement of heat from the surface, an associated increased activity of those powers by which heat is produced ; so that the former is more than compensated by the latter. In order to bring this view into harmony and connexion with Virchow's well-known doctrine of an inhibitory centre situated somewhere in the intra-cranial nervous system, all that is necessary is to suppose that just as in clinical fever the influence of this centre is directly paralysed by the morbific agent, so after section of the cord its influence on the tissues is annulled by the severance of the channels by which it is normally exercised.

It is, fortunately, no longer necessary to occupy space in discussing the theory according to which there is a direct physiological relation between the nervous system and the chemical processes on which the production of heat depends ; for it has now been shown experimentally by Dr. Murri that after severance of the cord, the temperature rises even when the thermogenetic function may undergo a very great diminution. As, therefore, there is no increase of production, the hypothesis of increased discharge, which is necessarily associated with that of increased production, falls to the ground of itself. Dr. Murri has, however, by another series of researches, furnished us with the direct proof that no such increased liberation of heat takes place. It is a fundamental and well known fact in relation to the distribution of temperature in the animal body, that the greater the vigour of the circulation, the less is the difference of temperature between the central and superficial parts, so that by measuring simultaneously the temperature of the skin and that of the rectum, we are enabled to judge very accurately of the velocity of the blood stream. Why this is so, is easy to understand. When the arteries are distended, and the blood current is rapid, a larger quantity of blood is brought to the surface from the warmer central parts of the body than in the contrary case. The mass of blood therefore being greater, the cooling it sustains by exposure to the cooler environment of the body is proportionately less, so that it returns by the veins towards the centre at a temperature which does not differ largely from that which it possessed in its outward course. Consequently if we find the temperature of the surface much less than that of the central parts, we are quite certain that the circulation through the surface vessels is feeble, and that little heat is being given off. Now Murri found that, even when after section of the cord, the internal temperature was normal or excessive, that of the skin was unnaturally low, a proof that the condition of the circulation was such as to be least favourable to the discharge of heat from the surface.

The hypothesis of increased exchange of heat having been got rid of, we fall back on the one fact of which the importance has already been indicated as affording the most striking characteristic of the thermal state of an animal after section of the cord, namely, that the bodily temperature yields with abnormal facility to the influence of outside conditions—that the temperature equilibrium, to use Naunyn's expression, becomes labile. This being the case, it is obvious that the analogy between this condition and that of fever is not sufficiently close to justify

us in following the example of those pathologists who have founded on it a theory of fever. As, however, it may be of use in enabling us to answer some inevitable questions, and particularly may facilitate the understanding of the relation between thermogenesis and temperature in fever, time will not be wasted in instituting a comparison between the two kinds of pyrexia.

In the various fevers which form the subject of clinical observation, no very accurate information exists as to the state of the circulation. The comparison of the central with the surface temperature, which in the study of the effects of section of the spinal cord, affords us such valuable information, would also be of value if it were made in the early stage of fever but as yet clinicists have not recognised its importance; so that the necessary basis of observation is wanting. In the later stages of fever the introduction of another element, that of sweating, a heat-discharging process which is in great measure independent of the circulation, deprives the observation and measurement of the surface temperature of much of its value as a criterion.

As regards thermogenesis it must not be supposed that in fever the diminution of this function is comparable in degree to that which occurs after section of the cord. In the first part of this paper it has been shown that as regards the ordinary sources of heat, viz., those dependent on the ingestion of food, the diminution is so considerable that the total quantity of heat produced in the body in a given time, even when augmented by the quantity arising from the abnormal disintegration of tissue, may still fall short of the average of health. This being the case, it is natural to ask, how it is that we do not meet with instances of fever in which, (as after section of the cord in small animals and under external conditions favourable to cooling,) the temperature remains stationary or sinks instead of rising. The answer to this question is, that although, as might be expected, we have perhaps no counterparts in human pathology to these relatively common cases in which, after accidental injury of the cord, the patient becomes cold instead of hot, such instances are familiar to the experimental pathologist. We have seen that in the dog febrile pyrexia may be induced with certainty by the introduction into the circulation of a known dose of pyrogenic substance. If a dose of the same substance, proportionate in quantity to the smaller weight of the animal, be injected into the circulation of a rabbit or guinea pig, the same succession of disorders occurs with this difference, that the temperature falls *below* the normal instead of rising above it, the amount of depression varying according to the temperature of the environment. Here, namely, just as after section of the cord, we have evidence that the thermogenesis *may fall below the normal limit of adequacy*: the cause, which in a larger animal would produce fever with all its signs, here produces only an intense general disorder with diminished heat of body and diminished thermic discharge.

e.—Concluding Inferences as to the Seat of Origin of Febrile Pyrexia.

A satisfactory explanation of the nature of fever and of its relation to the febrile process is not at present possible, because we are not as yet possessed of the necessary physiological knowledge. We have elsewhere stated that two possibilities are open to us. One is, that fever originates in disorder of the nervous centres, that by means of the influence of the nervous system on the systemic functions, the liberation of heat at the

surface of the body is controlled or restrained, so that "by retention" the temperature rises, and finally that the increased temperature so produced acts on the living substance of the body, so as to disorder its nutrition. The other alternative is, that fever originates in the living tissues, that it is from first to last a disorder of protoplasm, and that all the systemic disturbances are secondary.

In both hypotheses it is tacitly assumed that fever is the product of a material fever-producing cause contained in the blood or tissue juice, the morbific action of which on the organism is antecedent to all functional disturbances whatever. At bottom we are all humoralists, and believe in infection. It is not until we have to say where and how the infection acts that questions arise.

The facts and considerations we have had before us are, I think, sufficient to justify the definitive rejection of the first hypothesis in all its forms; for, on the one hand, we have seen, that no disorder of the systemic functions or of the nervous centres which preside over them is capable of inducing a state which can be identified with febrile pyrexia; and, on the other, that it is possible for such a state to originate and persist in the organism after the influence of the central nervous system has been withdrawn from the tissues by the severance of the spinal cord.

We are therefore at liberty to adopt the tissue-origin of fever as the basis on which we hope *eventually* to construct an explanation of the process. But if we attempt to do so *now*, we shall at once find ourselves in face of an unsolved physiological problem, that of the normal relation between temperature and thermogenesis, for the elucidation of which it is necessary to investigate, much more completely than has yet been found possible, the influence of temperature variations on those chemical processes in living tissue, with which thermogenesis is necessarily associated. The little that has been already accomplished in this direction is sufficient to show that the living substance of our bodies is, if I may so express myself, delicately sensitive to variations in the temperature of its environment, so that very slight deviations from the normal may produce effects of surprising magnitude.

No. 2.—Dr. J. Burdon Sanderson's Reports of an experimental study of Infective Inflammations.

A.—Report of 1872.

App. No. 2. On Infective Inflammations, by Dr. Burdon Sanderson.

Introduction.

When a living tissue is injured mechanically or chemically without being destroyed, it becomes the seat of a succession of changes which are the products of the disorder of the vital functions of the injured parts. These changes collectively receive the name Inflammation. The term comprehends, therefore, an assemblage of phenomena, held in relation with each other by the circumstance that they are all effects of the same injurious agency, and that they all form parts of one process, of which the various stages follow each other in more or less orderly succession.

Inflammation is the reaction of a living tissue against an injury.

It is not needful, in introducing the present inquiry, to describe the process of inflammation, for the question which concerns us has relation rather with the agency by which the phenomena are produced than with the manifestations of its action. It will be sufficient to remind the reader that the phenomena are of two kinds—those which depend on changes in the structural elements of the tissues, and those which have their seat in the blood-vessels; and that the latter, again, admit of a very obvious division, into those which concern the blood-vessels as muscular tubes (the contractile elements of which are under the immediate control of the vaso-motor nervous system), and those which relate to their function as mere conduits for the conveyance and distribution of blood.

If we compare these two orders of phenomena (the vascular and the textural effects of injury) with reference to their importance as characteristics of the process of inflammation, we shall assign the first place to the former, leaving the latter in subordinate and consequential relation to it; for although we know that a living part cannot be injured without the elements of its tissue undergoing those germinative changes of which the production and multiplication of young cells is the result, yet observation teaches us that this cell germination is never the first link in the chain of effects of which the reaction of a living tissue against an injury consists.

Of the two kinds of local changes of which inflammation consists (textural and vascular), the former are subordinate and subsequent to the latter.

The first local effect which an injury produces in a living part is vascular; it manifests itself as above indicated in two directions simultaneously. On the one hand, the state of contraction (or tonus) of the smallest arteries is altered or modified within and around the seat of injury in such a way as to determine increased supply of blood to the injured part; on the other, the walls of the capillaries undergo imperfectly understood changes, by virtue of which the liquor sanguinis (plasma) and corpuscles sweat or squeeze out into the lymphatic spaces in which the elements of the tissues lie.

This sweating out of the liquor sanguinis we call exudation, using the term in its original and etymological sense as distinguished from that which has been more recently given to it. Shortly after the introduction of the microscope as an instrument of pathological research, the microscopical study of the cellular products of inflammation so completely engrossed attention that by many writers the process or injury by which

The act of exudation is the link between the vascular and textural changes.

they were produced was altogether forgotten or left out of sight. So much so is this the case that in some of the best known text books of 20 years ago the word exudation is used as a name for certain sorts of liquids (purulent, tuberculous, &c.), or for the cells which were then supposed to characterise them. On this account it is necessary to state that by exudation we mean the act of exudation and not the liquid resulting from that act.

The question of the relation between this act and the textural changes which are associated with it in the process of inflammation may, in accordance with what has preceded, be thus stated:—The tissue elements begin to germinate because they are stimulated, but the exciting action may be either identical with that by which the process is originated, or a secondary consequence of that action; in other words, the tissue may be acted on directly by the mechanical or chemical cause of the inflammation, or mediately by the flood of exuded liquor sanguinis with which it is irrigated. I have elsewhere stated* why it appears to me probable that in most inflammations the excitation of the tissues is indirect or secondary. This inference is mainly founded on the consideration that whereas we know of no instance of germination of tissue without exudation preceding or accompanying it, it can be proved by experiment that the introduction of exudation liquid into a healthy living part at once determines germinative changes. Admitting the facts, the proof is still incomplete, for it is not denied that there may be examples of textural germination occurring under the immediate influence of mechanical or chemical irritation without any antecedent exudation. If such instances exist they are at all events exceptional.

The notion that the liquid which is exuded in an injured part, as the immediate result of the injury, is itself the exciting agent by which the ulterior and more obvious changes are determined, appears at first sight to stand in very close relationship with the subject of the present inquiry; for if we say that all inflammatory liquids, even those of the most simple inflammations, are endowed with the property of irritating or exciting the elements of the tissues with which they come into contact, it seems very much the same as if we were to say that all inflammations are infective or contagious. If the word infective were to be understood as merely signifying the injurious action of a diseased product on healthy tissue, infectiveness would certainly be an attribute of every phlegmonous liquid. The difference in this respect between one inflammation and another would be merely a question of degree. But before accepting such a view of the subject, which, however logical it may appear, carries with it something which is opposed to experience, we must carefully consider whether the definition above referred to truly expresses the sense in which the word infective is intended to be used.

Definition of the term "infective" in its application to the products of inflammation: —Equivalent expressions in common use.

In the current language of the bedside it is usual to speak of inflammations being "healthy" or "unhealthy," and to distinguish between *pus bonum et laudabile* and other sorts of pus to which these favourable adjectives cannot be applied. The characters by which the good or bad quality of a purulent liquid, or the healthy or unhealthy conditions of a wound or granulating surface, may be distinguished are plainly set down in practical works, and thoroughly appreciated by every practical surgeon; and it is also well understood that unhealthy inflammations are not only distinguised by their objective characters, but also by the property which they have to produce general disorder of the health of the patient, and in their turn to be injuriously affected in their progress

* "The Process of Inflammation." Holmes' System of Surgery, 2nd Edition, vol. v., p. 786.

Inflammatory or traumatic fever.

by the disorder they have themselves produced. The constitutional state which is associated in this twofold way with inflammation as its product and its cause, exhibits variations which do not always correspond either with the extent or even with the intensity of the local process which it accompanies, and receives names which express that variation. It may be admitted that in all cases inflammation, if of considerable extent, is attended with fever; but there is a marked difference between the slight febrile disturbance which accompanies healthy suppuration and the degrees of general disorder which are expressed by such terms as "irritative fever," "pyæmia," or "septicæmia." These three, or the constitutional states that are associated with them, pass into each other by insensible gradations, but are separated from health by a line which has become much more easy to define practically at the bedside since the thermometer was introduced into every-day use as an aid to clinical observation.

To distinguish those inflammations which produce grave constitutional disturbance and secondary lesions, by an expressive word we call them *infecting*. In using the term we are guided by the same criterion as those on which the surgeon bases the practical distinctions above referred to. An inflammation which is more or less exactly limited in duration and extent by the limits of the injury which has caused it, may, with scientific precision, be designated a simple or normal inflammation. An inflammation which spreads and endures beyond the direct and primary operation of its cause, which induces similar inflammations in other parts, and disorders the vital functions of the whole body, has in it something beyond the effects of the injury, and may properly be termed *infective*. Thus infectiveness is marked by two sets of characteristics, one relating to what occurs at the original seat of inflammation, the other to the induced effects which manifest themselves elsewhere. Of the two groups of phenomena it is obvious that those which are removed from the seat of action claim most attention, for they afford evidence that material must have been discharged from the original focus, either by the absorbents or the veins, into the circulation. They consist partly in the springing up of new foci of inflammation along the course of the infected channels (the anatomical distribution of which secondary foci always distinctly indicates the source from which they have originated), partly in the occurrence of changes in the physical and organoleptic characters of the blood itself (not as yet investigated), of such a nature as to show that it is impregnated with the infective poison.

Previous observations showing that an inflammation may give rise to two infective processes, which, although associated in their origin, differ in their development. Of these, one is chronic, the other acute.

In the extended series of experiments made by the author in 1867 and 1868, one branch of the question of phlegmonous infection was worked out with some completeness. It was then found that when in the lower animals local inflammations are produced either in the skin or peritoneum by the introduction of irritant substances, two distinct sets of consequences manifest themselves, viz.: (1) a chronic disease exhibiting in all respects the anatomical characters of tuberculosis, and consisting essentially in the overgrowth of certain tissues then designated as lymphatic or adenoid, and shown to be in close relation with the lymphatic system; and (2) an acute disease presenting the leading features of pyæmia, attended with the formation of metastatic abscesses, and as a rule terminating fatally either very rapidly by intense peritonitis without any other appreciable lesion, or more slowly by the formation of infective abscesses and nodules, associated with inflammation not only of the peritoneum, but of other serous cavities.

These two morbid processes, the chronic and the acute, are both infective in the sense in which the word has been defined above, both

apparently spring from an infection derived from the same source (that is from the same primary infective focus), and progress in the same animal at the same time. These facts afford, however, no sufficient grounds for regarding the two processes as identical, for notwithstanding the closeness of their relation to each other, the differences cannot be overlooked.

Reasons for regarding these as essentially distinct.

The first reason for considering the two processes as different is to be found in the fact that, to a certain extent, either may be produced independently of the other at the will of the experimenter. In my former paper I showed that if an extremely small quantity of material from an enlarged and indurated gland of a tuberculized—*i.e.*, chronically infected—guinea-pig is injected into the pleura of another animal of the same species, it may happen that no appreciable constitutional disturbance is produced at the time, and so little local effect that if the animal is killed within two or three weeks after the inoculation no trace of lesion can be detected in the pleura or elsewhere. Eventually, however, the animal becomes tuberculous, the process beginning by the enlargement of the minute lymphatic masses of the pleural serosa.* More conclusive ground for regarding the two processes as pathologically different is to be found in the difference of their development. The acute affection attains its acme shortly after the infection, and associates itself in its progress with the primary inflammation produced at the seat of injury by the introduction of the infective agent. The chronic affection, when its phenomena are not complicated and modified by being mixed up with those of the acute, progresses so gradually that the appearance of the lesions seems to be preceded by a period of latency, during which the seed, so to speak, fails to germinate. Not that it can be supposed that the infective material is really latent, but that the earliest changes are so inconsiderable that they cannot be readily discovered.

The experimental results now to be reported relate entirely to acute, *i.e.*, pyæmic infection.

Modes of investigation.

General description of the results.

The investigations on which I have now to report enable me to state more clearly than I could before what is the true relation between these processes. The experiments differ from those referred to above in two important respects. In the first place, the material employed for exciting the primary inflammation was, as a rule, a product of an acute process; and secondly (what is of much greater importance), the quantity used for each insertion was ten or twenty times as large. Consequently in all cases the results obtained were, if the expression may be allowed, pyæmic rather than tuberculous. The animals were affected at once, suffered as a rule from well marked constitutional disturbance from the first, and died with or of intense inflammation in the serous cavities. The comparison of the lesions observed in these animals with those above referred to shows that in the acute cases, provided they live long enough, disseminated nodules are to be found in the serous membranes and in the substance of the abdominal and thoracic viscera, which soon assume the character of abscesses, and have the same, or at all events a very similar, distribution as the miliary nodules of the chronic process. They differ, however, alike in their prevalent characters and aspect, in their size, in their duration, and in the changes which they undergo.

Instead of slowly growing as if they were tumours, lasting for months in the vascular state, and eventually dying at their centres by a process of caseation as gradual as their growth, they enlarge rapidly, are soft from the first, and eventually assume the character of abscesses. We must, however, guard against the assumption that there is any original structural difference between the rapidly growng and suppurating

* Recent Researches on Artificial Tuberculosis. 1869. Pp. 1, 5, 7.

nodule and the slowly formed caseating granulation, for both originate by overgrowth of pre-existing elements—in other words by germination.* The difference between them is not one of origin or even of structure, but of duration and development; the one grows as if it were a part of the tissue from which it springs, until by the redundant multiplication of its closely packed elements, its central parts lose their blood supply; whereas the other becomes itself the seat of an acute inflammatory process. The conversion of a granulation into an abscess is I think perfectly parallel to the change which the granulating surface of a wound undergoes under the same conditions, *i.e.*, when it assumes the unhealthy character. Just as the newly formed vascular granulation softens and breaks down by a process of inflammation determined by the change which has taken place in the constitutional state of the patient, so we may readily understand that when the inoculated animal becomes the subject of infective fever, the interstitial indurations and granulations which would otherwise have retained their vascularity, firmness, and transparency for many months, may become acutely inflamed and become the seat of abscesses.† In like manner in phthisis pulmonalis in man the local condition of the diseased organ not merely determines the constitutional state, but is afterwards affected by it; so that the setting up of irritative fever from whatever cause determines the softening of parts which would otherwise have remained in a state of chronic induration.

A chronic, *i.e.*, tuberculous infective process becomes acute, *i.e.*, pyæmic under the influence of infective fever, adventitious tissues of all kinds being more prone to suppuration than normal ones.

In my introductory report on the intimate pathology of contagion, published in 1870, I brought together the general grounds which exist for the belief that the *materies morbi*, or contagium of contagious diseases, in general does not consist of substances chemically dissolved in the morbific liquid. The direct evidence in favour of the proposition was to be obtained from experiments which proved that in the case of some of the best known examples of infective action the toxic agent could be shown to be incapable of diffusion, and therefore in the strict sense insoluble. It was further argued, in the second part of the same paper, that if infective agents are particulate they are probably comprised in that group of bodies to which I then applied the term microzymes—recognizing their indentity with the zooglæa of Cohn, the micrococci of Hallier, and the various forms described by other authors under the terms *bacterium* and *vibrio*.

Existence of microzymes in the exudation-liquids of infective inflammations and in the blood of infected animals.

With reference to these organisms, two entirely new and most important facts have been demonstrated by the observations to be now recorded. It has been discovered (1) that in all acute infective inflammations microzymes abound in the exudation-liquids; and (2) that the same forms are also to be found in the blood of the infected animals, their presence being a constant accompaniment of all acute infective suppurations.

The more detailed statement of these facts will be found in the account to be immediately given of the experiments. It will, however, be convenient, in order to facilitate the understanding of that description, to explain here certain words which we have been in the habit of using to designate the varieties of form which are most frequently met with according to their grouping and mode of growth. These organisms present, in the exudation-liquids, characteristic appearances to which we apply various terms, such as colonies, bacterium filaments, dumb-bells and chains. The word *colony*, first introduced by Hallier, is used to

Explanation of certain words used in describing the microzymes of infective liquids.

* For reasons given in a former report I prefer the word germination to proliferation, used by many writers to express the same idea.

† It has not yet been proved experimentally that it is so.

designate groups of well defined contour, in which the individual microzymes are held together by their interstitial substance, which in this case forms a transparent matrix in which the rods and spheroids are embedded. A *bacterium filament* is simply a row of rods arranged end to end. A *dumb-bell* consists of two spheroids connected together by a bridge of envelope substance. A *chain* consists of a series of dumb-bells arranged end to end. Intermediate forms between dumb-bells and chains and rods or bacteria occur, which may be called *varicose rods.*

We have found it practically more convenient to use these common words* than to apply to the forms the specific designations used by morphologists, *e.g.*, *zooglœa* for colonies, *bacterium varicosum* for dumb-bells, *bacterium termo* for rods, &c.

As regards the morphological relation between these forms, I have little to add to what was stated in the last report. It is probable that they are organically continuous forms, but we are not in a position to state the precise relation in which they stand to each other.

It is, however, possible to divide them into two groups according to the circumstances under which they occur and thus to establish a classification, which, whatever may be its morphological significance, is of interest pathologically. Of these groups the rod is the type of one, the dumb-bell of another. In liquids in which the development of microzymes is going on with very great rapidity, as *e.g.*, in the exudation-liquid of intense infective peritonitis, single rods are found which are extremely minute, not larger than $\frac{1}{1000}$ millimeter in length. The less acute the process the larger the rods, and the more they are arranged in filaments end to end. In exudation-liquids, *e.g.*, in the liquid of a subcutaneous abscess, or of a peritonitis which has lasted for some weeks, there are scarcely any rods ; the prevalent forms are spheroids, dumb-bells, and chains.

The observations relating to exudation-liquids have entirely confirmed the conclusion arrived at in my former report with reference to the microzymes of ordinary drinking water, that they do not either originate from fungi or develop to them. On no single occasion has any form of mycelium been discovered in any of the innumerable infective liquids, charged with microzymes which have been examined.

Section I.—Previous Experiments on Acute Infection.

Before proceeding to bring under the notice of the reader the important results of the inquiries of the past year to which reference has just been made, I propose to give an account of some investigations made at former periods relating to the same subject.

Experiments in 1867.

In the year 1867 various experiments were made for the purpose of comparing the effect of inoculating various pyæmic or septicæmic liquids with those obtained by the insertion of minimal quantities of chronically indurated lymphatic glands or other products of chronic infection. I transcribe the notes of some of these experiments.

Aug. 23rd, 1867. Three guinea-pigs and a dog were inoculated with purulent liquid from the ankle joint of a patient affected with pyæmia. The patient, a man aged 28, was admitted into Middlesex Hospital under my care on the 20th of August, in a state of extreme typhoid depression. He complained of pains in all his joints and there was

* Since the above was written, Professor Cohn, of Breslau, has proposed an improved classification and nomenclature of bacteria, which will probably be in future generally used by pathologists. See his "Beiträge zur Biologie der Pflanzen," pp. 127–224.

effusion in the left knee and ankle. The day after his admission he had swelling and inflammation at the root of the nose which subsequently extending to the eyelids. The inflamed parts were soon covered with phlyctenæ, which rapidly suppurated and a fœtid discharge from the nostrils commenced. During the next day subcutaneous suppurations presented themselves in various parts, particularly in the left arm and right leg. In these situations the skin was swollen and livid, while numerous phlyctenoid pustules appeared in the neighbourhood. Death occurred during the following night. At the post-mortem examination the pustular eruption was found to consist of separate pustules and of confluent groups, both of which were more abundant on the face, and especially around the nose than elsewhere. There was an abscess in relation with the middle third of the left clavicle which extended outwards for two inches behind and below the bone ; no part of which, however, could be ascertained to be in a rough or denuded state. All of the subcutaneous abscesses, of which a considerable number were examined, were found to be lined by a thin but distinct membrane. Diffuse purulent infiltration was not found in any part of the body. The serous surface of the pericardium exhibited hæmorrhagic patches, and the blood contained in the cavities of the heart was uncoagulated ; it coagulated, however, when placed in a tube. Five or six nodules of grey induration were found under the pleura near the apex of the right lung, each being surrounded by apparently healthy lung tissue, and covered by healthy pleura. Other similar sub-pleural nodules were met with in the middle and lower lobes, but in the latter instead of being grey throughout they were blood-stained externally, so that the outer part resembled on section an apoplectic mass. In the left lung the nodules were smaller and less numerous. The abdominal organs exhibited no morbid appearances excepting those of hyperæmia. The blood was examined microscopically and found not to contain an excess of colourless blood corpuscles. In this case the pyæmic infection seemed to originate from the abscess near the left clavicle. The patient had complained of pain in this situation for ten days before any other symptoms presented themselves, during which time he was so free from constitutional ailment as to be able to attend to his occupation. He then began to suffer from pain in the joints, but had no serious symptoms until two days before his admission into the hospital. From the peculiar localization of the cutaneous cellulitis and pustular erruption, and the fœtid coryza, I at once inferred that the case was one of acute glanders ; but on careful inquiry found that the patient's mode of life was such as almost to preclude the possibility of this origin of the disease.

The first of the infected guinea-pigs died 15 days after inoculation. The inoculation was performed in the usual way, care being taken to use a very small quantity of liquid. The animal was found on the 7th of September with hurried and difficult breathing and loss of power of the hind legs. It was at once killed. The dissection is noted as follows :— Wound : a large abscess, of very irregular form, exists at the seat of inoculation, measuring at its greatest diameter no less than two inches ; it is lined by a well defined but thin membrane and contains caseous pus The scapular glands are not in the slightest degree enlarged and are perfectly transparent. The other sub-cutaneous glands are also healthy. Two of the mammæ are much swollen and are found when cut into to be infiltrated with pus which is partly creamy, partly caseous. Lungs healthy. The liver contains hard nodules as large as pin heads, which are scattered over the convex surface of the right and middle lobes. The spleen is much enlarged. Five or six nodules, varying in diameter from half a line to a line, project from its convex surface. Both the nodules

in the liver and those of the spleen, have the character of abscesses: they have firm capsules and contain pus which cannot be distinguished from that contained in those underneath the skin; they lie for the most part immediately underneath the serous membrane.—The second guinea-pig died 20 days after inoculation.* A large abscess exists at the seat of inoculation; a similar abscess is found over the gluteal muscles of the right side, containing creamy pus, enclosed in an extremely thin capsule, the surrounding tissue being slightly hyperæmic, but not indurated. There is a third abscess between the intercostal muscles and the pluera, which projects into the pleural cavity. The axillary tracheal and submaxillary glands are natural: the inguinal glands on the right side are slightly enlarged. On the surface of the lower lobe of the left lung there is a nodule of consolidation. On cutting into it, it is found to be intensely hyperæmic, and to have the characters of pneumonic consolidation. A layer of false membrane adheres to its pleural surface. Besides this there are grains of much firmer consistence which project above the pleura. Of these, four can be counted on the lower and one on the upper lobe, while in the right lung a group present themselves near the outer margin of the lower lobe. One of them, larger than the rest, contains creamy liquid in its centre. On the convex surface of the liver, nodules similar to those described in the other animal exist. The spleen is enlarged.—The dog, a small terrier weighing 8 lbs., died 49 days after inoculation, in a state of great exhaustion and emaciation. The inoculation wound could not be discovered, and the sub-cutaneous lymphatic glands were healthy. The lesions of the internal organs were as follows:—With the exception that minute hard nodules are disseminated over its convex surface, the liver appears to be healthy. The spleen is much enlarged, and contains groups of pale grey nodules in considerable numbers. The organ is adherent to the anterior wall of the abdominal cavity, as well as to the omentum and diaphragm, by softish false membranes, and the whole organ is covered with a layer of soft "lymph."—From one of the guinea-pigs two others were inoculated, both of which died within 48 hours after inoculation. Pus taken from the seat of inoculation was used to inoculate two others; one lived a month, the other 45 days. In both there were multiple abscesses under the skin; in the one which lived longest the right lung exhibited nodules and patches of lobular condensation with pleural adhesions. In the other the internal viscera were healthy.

On the 15th of December 1867 four guinea-pigs were inoculated with purulent liquid from the knee-joint of a man who had died of pyæmia. The patient, aged 42, was admitted into St. George's Hospital on the 20th of July with disease of the right astragalus and os calcis. Pyæmic symptoms supervened on the 3rd of December, and he died on the 14th. The liquid was taken and used about 20 hours after death. It was of a pale yellow colour, and opalescent appearance. Many of the pus corpuscles it contained were charged with fat granules. [Nothing was noted as to the presence of bacteria.] Of the four guinea-pigs, No. 1 died on the 21st day, the appearances being as follows:—An open wound exists at the seat of inoculation—A discharged abscess. Around the wound and extending from it towards the middle line, are several abscesses, some of which are confluent. The scapular gland of the side corresponding to the wound is enlarged and contains pus. The other sub-cutaneous glands and the internal organs are healthy. No. 2 died

* Whenever the present tense is employed the wording of the original notes is used. It is, however, abbreviated.

on the 22nd day; it was inoculated in two places. Both wounds are open and have indurated borders. Numerous small sub-cutaneous abscesses are scattered over both flanks in the neighbourhood of the wounds. The right middle lobe of the left lung contains in its depth a hard nodule about two lines in diameter. There are one or two sub-serous nodules in the spleen. The other organs are healthy. No. 3 died on the 26th day. The wound is open and a cord of induration extends from it for three-quarters of an inch to an abscess which is in immediate contact with the scapular gland, lying between it and the wound. The abscess measures five lines in diameter, and the gland, which is softened and contains creamy pus, is nearly as large. The other sub-cutaneons glands are healthy. [In this animal the internal organs were destroyed by its companions, so that they could not be examined.] No. 4 died on the 27th day. A very large abscess exists at the seat of inoculation, and a smaller one in its immediate neighbourhood. The scapular gland of the same side is enlarged and softened. The internal organs are found, on scrupulous examination, to be healthy. —On the 18th of November a guinea-pig was inoculated with pus from a pyæmic abscess in the posterior mediastinum of a patient who died in hospital on the previous day. The bodies of several dorsal vertebræ were diseased, and their excavated and roughened surfaces formed part of the wall of the abscess. There were pyæmic nodules in the lungs and kidneys. The animal was killed 32 days after inoculation. An abscess three or four lines in diameter, containing creamy pus enclosed in a membranous capsule, exists at the seat of inoculation. The capsule is firmly adherent to the skin and panniculus. The subcutaneous lymphatic glands are not enlarged, and the internal organs are healthy.

Experiments in 1871.

To these observations made in 1867–8 I append another of more recent date.* A girl aged 16 was admitted into the London Hospital on the 3rd July 1870, with strumous disease of the bones of the little finger and great toe. On the 12th of January 1871 the diseased organs were removed. The wound of the foot healed favourably, but that of the hand became unhealthy. Pyæmic symptoms (infective fever) appeared on the 26th. On the 7th of February an abscess was opened in the neighbourhood of the elbow joint. Pus was collected in calcined glass tubes which were immediately sealed. The same day the pus so collected was injected into the peritoneal cavities of several guinea-pigs according to the following method. In each case a sharpened cannula previously boiled is first introduced through the anterior abdominal wall into the peritoneum. A capillary tube open at one end and expanded at the other into a closed bulb having been prepared, the pus is discharged into a calcined cup of glass, like that used for holding vaccine in my former experiments. The open end of the capillary tube is then dipped into the pus, and filled by capillarity to a certain distance. [If desired, the quantity taken up can be easily determined by the balance.] The charged end is then passed by the cannula into the peritoneum, and the bulb slightly warmed, by which means the whole of the pus is discharged.—Nine weeks after inoculation two of these animals were dissected. Both exhibited the same appearances. The lesions observed (in No. 1) were as follows:—At the seat of puncture there is a slight induration. The inguinal glands are enlarged and softened on both sides; the scapular glands are also somewhat enlarged; but the other subcutaneous glands are normal. The inguinal glands, particularly on the right

* This experiment is briefly referred to in my report for 1871.

side, are surrounded by zones of intense injection, and there are numerous minute abscesses disseminated under the integument in their neighbourhood. Another group of abscesses surrounds the internal inguinal ring. The peritoneum is distended with sero-sanguineous liquid, in which are seen active bacteria of small size but very distinct form. The omentum is beset with minute nodules. The centrum tendineum of the diaphragm also exhibits a few nodules. The liver weighs 35 grammes: it is very pale and beset here and there with nodules, some of which are purulent. The spleen is enormously enlarged. [Condition of mesenteric glands not noted.] The pleuræ and the pericardium contain exudation liquid. Groups of opaque grey nodules are scattered throughout the lungs, both in the depth and at the surface.

Comparison of the lesions observed in animals inoculated with pyæmic products, with those produced when the material inoculated was derived from chronic secondary indurations.

The observations related in the preceding paragraphs show that although, as already stated, there is a close correspondence as regards the distribution of the infective nodules of the internal viscera between animals infected with pyæmic products and those inoculated with equally small quantities of the material derived from chronic secondary indurations, the contrast between the results is very marked. I will refer first to the lesions, and secondly to the development and mode of termination of the two processes. — *Subcutaneous lesions.* When an extremely small quantity of chronically enlarged lymphatic gland is inserted under the skin, in the manner described in my former paper, no abscess is produced either at the seat of inoculation or in any other situation. The wound to all appearance heals; but if it is carefully examined many weeks after, it is found, provided that the ingrafting has been successful, that a group of semi-transparent nodules exists under the skin, which represent the centre of infection. In the pyæmic cases there may also be induration of the same nature, but the nodules assume from the first the character of abscesses, and are accompanied by groups of smaller abscesses, disseminated in the neighbouring tissue. In a considerable proportion of the pyæmic animals these primary and secondary metastatic subcutaneous abscesses were the only lesions found, even though the dissections were made many weeks after inoculation. *Visceral lesions.* In chronically infected animals (using the term for animals infected by the insertion of minimal quantities of fresh induration material in the manner set down in the preceding paragraph) the visceral changes are much more uniform and characteristic. To judge of the difference between them and the corresponding pyæmic lesions, the several organs must be separately referred to. (1.) The chronically infected liver (*see* Eleventh Report, p. 110) does not usually present any morbid appearance to which the term "nodule" could be applied. The organ enlarges uniformly by the growth of a semi-transparent glistening interstitial substance, which, as it follows in its distribution the portal canals and occupies the spaces between acini and groups of acini, has an arborescent, not a nodular form, although the tracts of adventitious tissue exhibit nodular enlargement. Even when the change does not extend to the whole organ, but affects only a certain number of lobes, the newly formed tissue retains what descriptive pathological anatomists call the infiltrated as distinguished from the disseminated arrangement. In the acute affection the liver lesion is characterized by the presence of disseminated nodules, firm externally, purulent internally. (2.) The difference between the tuberculous lung and the pyæmic lung is perhaps not so obvious, but the characteristic appearance of the semi-transparent "iron grey nodules" (*loc. cit.*, p. 114), their uniform distribution throughout the parenchyma of the lungs, and the absence of concomitant pleuritic exudation or false membranes, are

facts which render the contrast between the two conditions sufficiently decided. (3.) Another very important distinction may be based on the condition of the lymphatic glands: in chronic (tuberculous) infection the internal lymphatic glands always become diseased tertiarily. They enlarge and pass into the state of chronic fibrous induration (*see loc. cit.*, p. 103), eventually becoming opaque and caseous. These changes may be well studied in the bronchial glands and particularly in those which receive their tributaries from the liver, in respect of both of which it may be observed that during the first two or three months after inoculation the glands remain unaffected. It is not until the pulmonary or hepatic disease has made some progress that the corresponding changes in the glands begin. In the acute affection it is entirely different. All the lymphatic glands which are in relation with the inflamed serous membranes become the seat of acute enlargement and softening. In tuberculosis they do not undergo this change, because the serous membranes are not inflamed.

Contrast between the two processes as regards development, progress, and mode of termination.

If we turn our attention from the lesions to the development and mode of termination of the two morbid processes, the contrast appears to be even greater. The most striking fact in this relation has been already referred to, viz., that when minimal quantities of induration material are used, the graft apparently lies hidden where it was inserted for many weeks, producing neither local inflammation nor fever (*loc. cit.*, p. 105), It is not till weeks have passed away that it begins to show its effect, first by the enlargement of the lymphatic glands in relation with the centre of infection, and then by the slowly progressing changes above referred to in the internal organs. The fatal result may, as my former observations showed, be postponed to an indefinite period, the animal living on in apparent health so long as there are sufficient of its organs unspoilt by the disease for the continuance of their functions. When it dies the result is usually determined by the setting up of an acute infective process, manifesting itself in serous inflammations, in the rapid softening of the indurated parts, and in the formation of vomicæ or abscess-like nodules in the diseased organs. Consequently, if we wish to study the chronic alterations of the internal viscera as they are, we must not wait till the animal dies, for by doing so we are almost sure to find them materially modified by the acute inflammatory softenings which precede the fatal issue. Just as in human pulmonary tuberculosis, so in the artificial disease, death is not caused by chronic induration, but by the acute infective inflammations which supervene upon them, or to which they furnish the occasion.

Section II.—Experiments on Acute Phlegmonous Infection, made during the year ending 31st March 1872.

First experiments as to conditions determining the presence of bacteria in peritoneal exudation-liquids.

I have already stated that in an experiment made in the spring of 1871 it was found that in animals infected by the introduction of a minimal quantity of pyæmic pus into the peritoneum, with all possible precautions against contamination of the infecting liquid by contact with other media, the peritoneal exudation-liquid was found to be charged with bacteria. This result suggested an important question. The presence of microzymes might be either a characteristic of the pyæmic process, or a mere result of the intensity of the peritonitis produced. To determine this, experiments were made during the following month (May 1871) which consisted in inducing intense peritonitis by the injection, not of exudation-liquids, but of chemical excitants, particularly dilute

ammonia and concentrated solution of iodine in hydriodic acid. As regards the ammonia, precautions were taken to guard against contamination by boiling and cooling the liquids as well as the implements to be used immediately before injection. In the case of the iodine solution this was, of course, unnecessary. In every instance it was found that the exudation liquids, collected from 24 to 48 hours after injection, were charged with bacteria; whence it appeared probable that the existence of these organisms was dependent, not on the nature of the exciting liquid by which the inflammation was induced, but on the intensity of the inflammation itself.

Division of the experiments into two series. Series I.—Experiments in which the exudation-liquids used were derived from infective inflammation of rapid progress.

After an interval of several months, occupied in other investigations, the inquiry was resumed. The experiments made may be divided into two series; in one those are comprised in which the liquids of acute infective inflammations were used, and consequently the results exhibited those characters of intensity and virulence which are expressed by the term septicæmia; in the others the results resembled those which have been already referred to in the preceding section, both as regards the methods and the phenomena induced. The important conclusions to which they have led will be stated after the facts themselves have been discussed. The following is a tabular summary of the experimental results of the first series :—

TABULAR SUMMARY of TWENTY-SEVEN OBSERVATIONS relating to the action of the Exudation-Liquids of acute Infective Inflammations when introduced into the Peritoneum or into the Venous System.

Number.	Date.	Description of Exudation-Liquid used.	Designation of Test Animal.	Date of Dissection.	Duration of induced Inflammation.	Mode or Channel of introduction of infecting Liquid.	Quantity of infecting Liquid used. +	Result.
1	Jan. 9 -	Liquid obtained by puncture from the cavity of the uterus of a bitch affected with acute infective muco-enteritis and metritis. The animal was killed moribund, and immediately afterwards dissected. The liquid was charged with rods and dumb-bells.	Guinea pig 11	Jan. 10	c. 20 hours -	Peritoneum -	5 Div. (c. 6 m.)	Intense peritonitis; serous surfaces of stomach and intestines hyperæmic; sanguinolent exudation-liquid in peritoneal cavity. Exudation-liquid crowded with rods, along with a certain number of dumb-bells, chains, and colonies. Blood plasma particulate, the particles in tremulous movement.
2	Feb. 26	Purulent liquid from diffuse subcutaneous suppuration in groin of a rabbit, in which blood had been taken from the crural artery ten days before. The *plasma puris* is charged with rods and colonies of dumb-bells; the blood contains numerous minute rods, and here and there a dumb-bell. The animal was killed moribund, and imdiately dissected.	Guinea pig 28 *a*	Feb. 27	12 hours- -	Do. -	3½ Div. (4 m.) -	Intense peritonitis; exudation-liquid milky, crowded with minute rods.
3	,, 26	Do. do. do. -	Guinea pig 28 *b*	Mar. 12	16 days - -	Do. -	Do. - -	Intense peritonitis, with false membranes on surfaces of viscera, and extensive adhesions; intense pleuritis; infective nodules (abscesses) in the abdominal viscera and underneath the peritoneum. Serous exudation-liquids abundant, crowded with rods, and containing other forms in small numbers; that of the pleura exhibits the particulate character. The purulent liquid of the pyæmic nodules in the liver contains rods in numbers, along with dumb-bells and chains. Blood tenacious; it contains numerous minute rods.

Tabular Summary of Observations relating to the action of the Exudation-Liquids of Acute Infective Inflammations—*continued*.

Number.	Date.	Description of Exudation-Liquid used.	Designation of Test Animal.	Date of Dissection.	Duration of induced Inflammation.	Mode or Channel of introduction of infecting Liquid.	Quantity of infecting Liquid used. +	Result.
4 and 5	Feb. 28	Peritoneal milky exudation-liquid of 28 *a*.	Guinea-pig 30 *a* and *b*	Feb. 28	10 hours -	Jugular vein -	5 Div. (6 ♏.) -	Both animals became collapsed soon after injection. Intense peritonitis; exudation-liquid crowded with rods of various sizes.
6	Mar. 12	Pleural exudation-liquid of 28 *b* -	Do. 39 *a*.	Mar. 26	16 days - -	Peritoneum -	2½ Div. (3 ♏.) -	Intense peritonitis and pleuritis, with false membranes covering surfaces of thoracic and abdominal viscera; consolidation of both lungs; pericarditis; pleural and peritoneal exudation - liquids crowded with bacteria.
7	„ 26	Pleural exudation-liquid of 39 *a* -	Dog I. XVI. *d*.	- -	- - -	Do. -	5 Div. (8 ♏.) -	This animal, after exhibiting for several hours the phenomena of acute infection (*i.e.*, rigors, followed by collapse with vomiting and purging), rapidly recovered.
8	„ 20	Purulent liquid from diffuse subcutaneous suppuration produced by injection of 3½ ♏. of dilute liquor ammoniæ under the skin of a guinea-pig. The liquid was charged with minute bacteria.	Guinea-pig 49 *a* and *b*	Mar. 20	6 hours - -	Do. -	3 Div. (3½ ♏.) -	Both animals became collapsed shortly after injection. Intense peritonitis; clear yellow viscid exudation-liquid, crowded with minute rods.
9	„ 20	Do. do. do. -	Do. 49 *c*	„ 21	24 hours -	Do. -	Do. - -	Post-mortem appearances the same.
10 and 11	„ 21	Peritoneal exudation-liquid of 49 *c*	50 *a* and *b*	„ 22	Do. - -	Do. -	Do. - -	Intense peritonitis; exudation - liquid viscid, and crowded with minute bacteria.
12	„ 23	Peritoneal exudation-liquid of 50 *a*	Dog XV. *d*.	„ 23	6 hours - -	Do. -	15 Div. (18 ♏.)	Death preceded by collapse, cramps, vomiting, and diarrhœa. Peritonitis and hæmorrhagic gastro-enteritis.
13 and 14	„ 16	Purulent liquid from the enlarged and softened mesenteric glands of 42 *a*. (See p. .)	Guinea-pig 44 *a* and *b*	„ 18	2 days - -	Do. -	4 Div. (5 ♏.) -	Intense peritonitis; purulent false membranes on the serous surfaces of the intestines and abdominal viscera; exudation-liquid viscid, swarming with minute short rods. Mesenteric glands enlarged and softened; one of them contains a large abscess, the purulent contents of which are charged with bacteria.

Tabular Summary of Observations relating to the action of the Exudation-Liquids of Acute Infective Inflammations—*continued.*

Number.	Date.	Description of Exudation-Liquid used.	Designation of Test Animal.	Date of Dissection.	Duration of induced Inflammation.	Mode or Channel of introduction of infecting Liquid.	Quantity of infecting Liquid used. +	Result.
15	Mar. 18	Purulent liquid from the enlarged and softened mesenteric glands of 44 *a*.	Guinea pig 46 *a*	Mar. 19	24 hours - -	Peritoneum -	4½ Div. (5½ m.) -	Intense peritonitis; exudation-liquid crowded with minute rods; other forms distinguishable with difficulty.
„	„ 18	Do. do. do. -	Do. 46 *b*	„ 29	11 days - -	Do. -	Do. -	Intense peritonitis with adhesions; infective nodules in omentum, mesenteric glands, and viscera; exudation-liquid viscid and crowded with rods, which also exist in number in the purulent contents of the nodules.
16, 17, & 18	„ 19	Peritoneal exudation-liquid of 46 *a*	Guinea pig 47 *a*, *b*, & *c*	„ 20	12 hours - -	Do. -	5 Div. (6 m.) -	All three animals became collapsed shortly after injection. General peritonitis; serous surfaces of intestines intensely injected; viscid exudation-liquid, crowded with rods.
19	„ 19	Do. do. do. -	Dog, VI. *d*.	„ 19	4 hours - -	Do. -	10 Div. (12 m.) -	The same symptoms during life and appearances after death as in No. 12 (see commentary).
20	„ 20	The same liquid kept since the preceding day in hermetically closed tubes.	Dog, VII. *d*.	„ 20	4½ hours - -	Do. -	Do. -	The same.
21	„ 20	Do. do. do. -	Cat, VIII. *e*	„ 21	5 hours - -	Do. -	Do. -	The same.
22	„ 20	Do. do. do. -	Cat, IX. *e*	„ 21	About 12 hours	Do. -	Do. -	The same.
23	„ 21	Do. do. do. -	Dog, X. *d*	„ 21	About 6½ hours	Do. -	6 Div. (7 m.) -	The same.
24	„ 21	Do. do. do. -	Dog, XI. *d*.	„ 22	About 12 hours	Jugular vein -	5 Div. (6 m.) -	The same. Symptoms extremely marked, and morbid changes excessive.
25	„ 21	The same liquid diluted with ¾ per cent. solution of chloride of sodium.	Cat, XII. *c*	„ 22	Do. - -	Peritoneum -	20 Div. (24 m.) -	The same.
26	, 21	Do. do. do. -	Cat, XIII. *c*	„ 24	About 3 days -	Jugular vein -	10 Div. (12 m.) -	The same.
27	„ 22	Blood of XI. *d*. charged with bacteria.	Dog, XIV. *a*	„ 22	19 hours - -	Peritoneum -	15 Div. (18 m.) -	The appearances on dissection indicate a peritonitis of extreme intensity. Surface of stomach and intestines covered with purulent false membranes; omentum intensely injected, and in parts in a state approaching gangrene; intense muco-enteritis of whole intestinal tract. Pleuritis, with sanguinolent exudation-liquid. Blood viscid, containing numerous minute bacteria.

Commentary on the Table.

In the first eight vertical columns the circumstances relating to the introduction of the exciting liquid are stated; in the last column the result as regards the conditions of the serous membranes and internal organs, and of the blood. The liquids used as excitants were in each case exudation-liquids; they were injected immediately after removal from the living animal. Of the 27 experiments, serous liquids were employed in 18; liquids of subcutaneous suppurations in four; liquids from softened infective nodules and lymphatic glands in three. In one, blood of the infected animal was used; and another, the contents of an infectively inflamed uterus. All of these liquids were charged with bacteria at the moment that they were removed from the living animal. In the fourth column the test animals or re-agents, are designated by numbers; the Arabic numerals relate to guinea-pigs, the Roman to cats or dogs. The fifth column gives the time after inoculation at which dissection was performed. In most cases the test animals were killed for the purpose when *in articulo*, in order that the blood and exudation-liquids might be examined in the recent state. In a few cases the dissections were made immediately after the animals had died naturally. From the sixth column it appears that in four cases the infecting liquid was injected into the jugular vein; in the rest into the peritoneum. The quantities used varied from 3 minims to 24 minims (consequently they were always incomparably greater than those employed in my experiments of 1867–68, which never exceeded a fifth of a minim).

Results.

Although the liquids were similar, all being products of rapidly progressing infective inflammations, the induced results were not all of equal intensity. Of the 27 animals used as re-agents, 20 died or became moribund within 24 hours, the mean duration of life after infection being about 13 hours. The others lived various periods from two days to 16 days. The protraction of the fatal result in these instances cannot be attributed to anything special in the particular experiments, for the table shows that in other animals injected at the same time and with the same material, no such postponement was observable. The facts illustrate a general principle which we shall see otherwise exemplified—that if an animal survives the first outburst of infective fever, it may be many days before it is exhausted by the subsequent secondary inflammations.

Of the 20 animals which died within 24 hours after infection, all excepting three (two guinea-pigs and a dog) received the excitant in the peritoneal cavity. In these three, in which the exudation-liquid was injected by the jugular vein, the signs of serous inflammation were quite as decided as in the others. All the 27 animals had intense peritonitis, and in the two guinea-pigs injected by the jugular vein, both of which were moribund before the end of the day, it was just as intense as in any of the others. In the dog, in which the process was equally precipitate, it was specially noted that the changes observed on dissection happened to be more pronounced than in the animals of the same species which had received the same liquid directly into the abdominal cavity. Hence, although the local action of the exciting liquid cannot be regarded as insignificant, it is not the determining cause of the intensity of the peritonitis. This conclusion is confirmed by the observation that the pleura and pericardium were often as intensely affected by injections into the abdominal cavity as the peritoneum itself.

In cases which terminate rapidly peritonitis is pro-

From the fact that in all rapid cases of acute infection there is intense peritonitis, it might be surmised that the peritonitis is the immediate cause of death. Such an inference would be groundless and probably

erroneous. The symptoms which we recognise in the dog as those of intense infective fever, viz., collapse attended with vomiting and purging, manifested themselves so early in all the cases, and particularly in the animals which were injected by the jugular vein, that it would be difficult to regard them as secondary to the peritonitis. The rapidity and completeness of the recovery which takes place in some instances (*e.g.* in dog No. I.) after collapse of some duration affords additional ground for attributing collapse itself with its accompanying phenomena to the direct action of the infective agent.

probably not the immediate cause of death.

In all the very rapid cases the peritoneal liquid exhibited the same character. It was viscid, and coagulated imperfectly or not at all. It contained pus corpuscles, but they were relatively not numerous; the plasma (*liquor puris*) often exhibited a tremulous movement which under high powers is found to be due to the presence of minute rods. With lower powers particles cannot be distinguished; all that can be seen is the peculiar tremulous movement of the liquid, which, however, is sufficiently characteristic. In addition to this appearance, the liquid always contains other actively moving rod-like bodies, larger than the particles above mentioned, but still not greater than $\frac{1}{500}$ of a millimeter in length. In the most rapid cases dumb-bells and chains are mostly absent, but they soon appear if the peritonitis lasts long enough, or if the liquid is kept for a day in the warm chamber in a plugged eprouvette.

Microscopical characters of the peritoneal exudation-liquid.

In all the acutely infected animals to which the Table relates in which the blood was examined, it exhibited microscopical appearances which were characteristic and unequivocal. They were of two kinds, and corresponded to those already referred to as presenting themselves in the serous exudation-liquids. The blood plasma exhibited more or less distinctly tremulous movement of the particles above described, and contained short colourless corpuscles, often contained rods in their substance, and that the blood discs seemed to adhere to each other, the blood possessing a remarkable viscidity, the nature and significance of which will be a subject for future investigation.

Microscopical characters of the blood.

General account of the symptoms and morbid appearances.

The symptoms observed during life, and the changes found on dissection in acute phlegmonous infection, which terminate in less than 24 hours, differ considerably according to the animal used. In guinea-pigs collapse comes on very rapidly after injection, whether into the venous system or into the peritoneum. It is marked chiefly by loss of muscular power and diminution of temperature. After death there is intense peritonitis. In the dog or cat the phenomena are more marked. In some few cases the animal passes rapidly into the state of collapse, but more commonly an hour or two elapses before any very striking effect is observable. Among the earliest obvious phenomena are muscular twitchings and shiverings, which may come on during the second or third hour; but thermometrical measurements in the rectum show that the temperature rises from the first. The supervention of collapse is indicated by failure of muscular power. This is accompanied by retching and vomiting, which are soon followed by diarrhœa. The retching is associated with violent spasmodic muscular movements. As soon as the contents of the stomach have been expelled, a frothy greenish liquid of viscid consistence begins to be discharged. The diarrhœa is at first attended with tenesmus, but afterwards becomes colliquative. The alvine discharge is mucous, shreddy, and always more or less stained with altered blood. A few hours before death the temperature begins to sink, eventually falling below the normal; this depression begins soon after the accession of the more severe symptoms, so that the period at which the vomiting and purging come on with violence usually

Symptoms.

Post mortem appearances.

corresponds to the acme of temperature. The most important of the changes observed after death are those which correspond with the symptoms. There is intense muco-enteritis of certain sections of the intestinal tract, the parts chiefly affected being the duodenum and rectum. The cases in which the alterations are most marked, are those in which, perhaps from great endurance on the part of the subject used, the toxic action, although equally intense, has been resisted a greater number of hours, so that it has had more time to develop itself. In such cases the whole tract may be inflamed, but in general the changes are limited as above stated. The mucous membrane of the duodenum is uniformly and intensely reddened, and its cavity distended with a mucous, more or less blood-stained, frothy liquid, in which float large flakes of exfoliated epithelium. The state of the rectum is similar, the staining of the mucous membrane is as deep and uniform, but the liquid is of a darker colour. The jejunum partakes more or less of the same conditions; but the ileum is always freer from change than any other part. Peyer's follicles are sometimes enlarged. The peritoneum is always hyperæmic in the most severe cases, and particularly the protracted ones, the hyperæmia is intense, and there are hæmorrhagic spots particularly on the omentum and mesentery. The characters of the exudation-liquid have been already referred to.

Comparison of the post-mortem appearances with those of putrid infection.

These symptoms and appearances closely correspond, if they are not absolutely identical, with those of septic infection in the dog, *i.e.*, with those which are produced by the injection of putrid animal liquids into the venous system. To illustrate this, I take the following account of the post-mortem appearances in this kind of poisoning from the well-known research of Bergmann on this subject.* After the injection of 4 to 7 cubic centimeters (60 to 100 minims) of putrid blood carefully filtered into the venous system of a large dog, the animal dies in from four to ten hours, the fatal issue being preceded by collapse, vomiting, and diarrhœa. On dissection, says Bergmann (p. 14), "the "most important post-mortem appearances are those found in the "intestine," consisting in "intense reddening and swelling of the "mucous membrane." In general the alteration "does not extend to "the whole intestine, but affects the pyloric end of the stomach, the "duodenum, the upper coils of the jejunum." . . . "The intestine is "filled with reddish thick mucous, which strikingly resembles the rose-"coloured rice water of the cholera stool. The further down in the "intestinal tract the liquid is examined the darker is its colour, until "in the large intestine it assumes a dull brownish red tinge which is "identical with that of the last alvine dejections. The quantity of "transudation-liquid in the intestine is very considerable. Even when "the extent of morbid alteration is greatest, it is mostly seen in the "upper part of the small intestine, colon, and rectum; the middle part "of the small intestine is either quite free or very slightly affected. ". . . . The greater the intensity and extent of this genuine gastro-"enteritis, the larger is the quantity in which shreds of separated "epithelium are mixed with the intestinal contents, and the more "abundant the excoriations and exfoliations of the mucous surface." . . . "In the worst cases an enteritis of equal intensity extends "the whole way from the cardia to the anal orifice. The croupous "diphtheric affection asserted by some observers to exist, I have not

* Dr. E. Bergmann, Das putride Gift und die putride Intoxication. Dorpat, 1868.

" observed. It appears to me that the yellowish shreds which separate " from the mucous surface are merely bits of shed epithelium."

The agreement of this description so far as relates to the mucous membrane of this intestine is complete. There is, however, one point of difference. Bergmann did not as a rule observe peritonitis in his animals. He records, indeed, that the mesenteric vessels were distended with blood, and that there were "sugillations" both in the mesentery and omentum; but it was only in two instances that he found the peritoneum generally inflamed. In these animals the exudation is described as being of a dirty brown colour, and very abundant; from which it seems reasonable to infer that in many other cases the condition was not observed, for it is scarcely probable that if the peritoneum was, as a rule, normal, it would be found in these two instances so intensely affected. It is much easier to believe that the very inconsiderable exudations which usually present themselves were overlooked.

In all other respects the differences are too inconsiderable to require special notice.

The inference above derived from the comparison of the phenomena of septic infection in the dog with those of acute phlegmonous infection, as to their close relation with each other, is confirmed by the following experiment, in which guinea-pigs were injected with exudation-liquids which had been kept for six days at the temperature of the body. It is seen that the results produced by such a liquid in the putrescent state, are not distinguishable from those which it produces when injected fresh in the same manner.

14th March.— Purulent liquid obtained from the spleen of a guinea-pig, which had been diluted with three-quarters per cent. solution of common salt, and kept at a temperature of 40° C. since the 8th, was injected into the peritoneal cavities of two other animals of the same species, the quantity used in each case being six minims. Both were moribund on the 16th. In the first there was intense peritonitis, and the peritoneum contained the usual viscid exudation-liquid. In addition to this there was œdema of the whole anterior half of the trunk. The blood vessels were dilated and distended with stagnant blood, over a region corresponding to that of the œdema, and extending from the middle line towards either flank. Beyond this region the vessels were remarkably empty. Not only the peritoneal liquid, but that of the subcutaneous œdema, was crowded with bacteria. The same forms were to be found in numbers in the blood, the plasma of which exhibited the particulate appearance already so often referred to. In the second animal, with the exception of the subcutaneous œdema, the appearances were similar. The blood and exudation-liquids exhibited the same characters.

Series II.—Experiments in which the liquids used were derived from chronic indurations in a state of suppurative disintegration.

I have now to refer to the second series of observations in which the infecting liquids were not products of virulent inflammation, such as those described in the last paragraph, but of more slowly progressing inflammatory processes, chiefly characterized by softening and unhealthy suppuration, either of infective nodules or of previously consolidated or infiltrated tissues. In the three series of experiments which will be given as examples of the rest, the original source of the infecting material was the diseased lungs of human beings or animals affected with chronic pulmonary tuberculosis in the stage of softening. The animals thus infected served in their turn as sources for the infection of others, the liquids used being derived from softened pyæmic nodules or lymphatic glands.

Dec. 22. A dog died in the Hospital for Animals of pulmonary phthisis of long duration. The condition of the left lung and pleura is noted as follows:—

There is a patch of consolidation about half an inch in diameter, over which the pleura is firmly adherent. Other similar nodules exist in other parts of the surface of the organ. On making sections it is found that each of these nodules is softened at its centre, and that around each, the lung substance is infiltrated as well as disseminated "with "grey and yellow tubercles." Of the ramainder of the organ, the greater part is airless. The pleural cavity contains several ounces of clear liquid. Of the pleural exudation-liquid a few minims were injected into the peritoneal cavity of each of five guinea-pigs. Three others received a similar quantity of the purulent liquid from one of the softened nodules. The liquids were injected undiluted by means of a Pravas' syringe, the quantities used being relatively large. The animals were dissected respectively, 15, 23, 28, 34, 59, 66, 69, and 69 days after injection. The lesions were substantially the same in all, in every instance the serous membranes were inflamed and contained variable quantities of exudation-liquid charged with bacteria, in most cases there were extensive adhesions and false membranes; all of the organs contained infection nodules, which possessed the characters already described, being hard and firm externally with soft and purulent centres. The pus contained in them was always charged with microzymes both in the form of rods and in those of dumb-bells and chains. The latter forms prevailed most in those animals which had survived longest. In those liquids in which they were either absent or in relatively small numbers when the liquid was fresh, they multiplied rapidly when the liquid was placed for 24 hours in a warm chamber at the temperature of the body, while the rods seemed to undergo a corresponding diminution in numbers. This fact was observed very frequently in infective liquids so cultivated.

The contrast between the conditions observed in these experiments and those which characterise the chronic infection which is produced by the injection of minimal quantities of induration material is very striking. Here all of the lesions are the products of an acute process. This may be inferred from their characters, but we have a more positive ground for the conclusion that they are so in the fact that, in the animal which died at the end of a fortnight after injection, the infective abscesses in the internal organs were already fully developed, and that as regards the state of the serous cavities the appearances did not differ in any material respect from those which were observed in animals which survived 40, 50, or even 60 days. Clearly, if in the former case the mischief was done rapidly, we must believe that it was also done rapidly in the others, and that if we had had the opportunities of examining those animals which lived longest at the same early stage in the disease we should have found similar lesions. In either case we have to do with the products of a rapidly developed pyæmia, the lesions of which not only come into existence but attain their full development during the first few weeks after injection, the difference between the long cases and the others amounting to nothing more than that in the former the struggle was more protracted. Essentially the processes are the same. If one is acute, the other is.

The points of distinction referred to in the introductory section between acute and chronic infection (pyæmia and tuberculosis) are also well illustrated in the experiments now under consideration. Two perfectly conclusive facts may be referred to, in evidence that the process with which we are now concerned is not that which I described in my former papers. The one is that the lesions of the internal organs although

they accord with each other with the greatest exactitude as observed in the different animals of the same series, notwithstanding the differences of duration of the morbid processes, are entirely different from those described by me as characteristic of "artificial tuberculosis." The second is that, in the experiments now before us, the animals were the subjects of serous and other inflammations from the beginning, whereas in tuberculosis no lesion whatever is discoverable by microscopic examination until the fourth or fifth week after infection.

Dec. 30. Material derived from the lung of a patient who had died the day before of phthisis in the third stage, in the Hospital for Consumption, was injected into the peritoneum in three guinea-pigs, and under the skin in three others. The first three were dissected respectively, 29 and 44 days after inoculation, having either died of themselves or having been killed *in articulo*. The other two were killed, 24 and 68 days after injection. In the first three the lesions corresponded very closely with those already described. The pleura and peritoneum were inflamed and contained considerable quantities ef exudation-liquid. The liver, spleen, and lungs contained pyæmic nodules, and there were similar nodules in the mesentery, omentum, and centrum tendineum of the diaphragm. One of the abscesses in the omentum was of very large size. The purulent liquid from the nodules contained rods and dumb-bells in great numbers ; the latter were found as usual to have become much more numerous after the liquid had been kept for a day in the warm chamber. The same forms were seen in the pleural and peritoneal liquids. In all of these animals the blood was found to present the usual alterations. The plasma was particulate, the particles exhibiting the movement before described, and contained rods and dumb-bells. The other three experiments are of interest as showing how little the mode of insertion modifies the result as regards the internal lesions. They lived longer, but in other respects the morbid process was the same, and it is specially to be noted that the signs of pleural and peritoneal inflammations were quite as marked as in the others. Purulent liquid from one of the animals was injected im the usual way into the peritoneum of a healthy guinea-pig, which, on dissection three weeks later had peritonitis and infective nodules in the usual situations.

Feb. 27. A small female monkey died in the Hospital for Animals of pulmonary phthisis. The principal lesions were as follows :—In the thorax the morbid appearances are confined to the right side. The right pleura is everywhere adherent. The whole of the right lung, with the exception of the apex is either consolidated and airless, or beset with numerous disseminated nodules. These nodules are for the most part firm externally, but softened at their centres. Here and there, there are vomicæ. The peritoneum contains clear liquid, along the border of the colon there are several nodules varying in size from that of a pea to that of a hazel-nut. Of these the smaller are grey, the larger yellowish white on section. Similar but smaller nodules exist in the mesentery. In the liver there are numerous softened nodules as well as around the portal vessels. Purulent liquid from the pulmonary nodules containing microzymes of both forms was injected in the usual quantity into the peritoneal cavities of five guinea-pigs. The tests were dissected at periods varying from 30 to 43 days after infection. The post-mortem appearances, both as regards the serous membranes and the internal viscera, resembled in all respects those already described.

Conclusion.

Considering the complexity of the subject we have attempted to investigate, and the importance of the questions involved in it, it is

requisite to exercise extreme caution in drawing conclusions. There are, however, one or two propositions which may be stated with confidence as the results of our observations. It has been shown (1) that that combination of malignant fever with intense and destructive inflammations to which pathologists have rightly applied the term septicæmia, because it is known by experiment as well as by clinical observation to result from the existence in the blood of putrescent albuminous matter, may also be produced by the introduction, into the circulation or into the serous cavities, of small quantities of liquids derived directly from living tissues in certain states of inflammation; and that such states have the same distinctive characters as those which distinguish inflammation of septicæmic origin. (2) That pyæmia (the term being understood to denote a general febrile disorder of less virulence than that of septicæmia accompanied by numerous disseminated inflammations, characterised chiefly by their proneness to suppuration) is so closely related to septicæmia as regards its origin and essential nature that in these respects no line of distinction can be drawn between them; and that pyæmia, like septicæmia, may originate from a purely traumatic inflammation, independently of any infection with contagium derived from a previously existing pyæmic inflammation. (3) That both of these conditions are characterised by the existence of microzymes in the infected liquids; and that the relation of intensity between different cases of septicæmia and pyæmic infection is indicated by the number and character of these organisms; so that in the most intense processes, *i.e.*, those which exhibit the characters of septicæmia, the exudation-liquids and the blood are crowded with actively moving bacteria, while in the more chronic processes, the spheroidal and dumb-bell forms prevail, and the numbers of organisms found in the liquids are relatively inconsiderable.

Among the more important of the further considerations of inquiry which our researches suggest, are the relations between pyæmia and other states of disease, and particularly ordinary inflammation, and the relation of pyæmic or infective fever to the local inflammations with which it is associated.

The fact that ordinary traumatic inflammation may pass by an apparently gradual transition into a pyæmic or septic one, is evidence that the distinction is not always obvious, but does not prove that it is ill-defined or vague. For although it may be extremely difficult to say precisely when infective characters begin to manifest themselves, yet, if we are entitled to assume that the appearance of those characters is an evidence that an infective substance or contagium which was not there before, has come into existence in the blood or tissues, there must have been a moment at which that substance was introduced, and consequently a moment at which the process would have to be regarded no longer as the effect of the injury, but as the combined effect of the injury and the infection. In this way it is conceivable that the line between healthy and unhealthy inflammation may be in reality sharply defined, however faint and difficult to appreciate.

In our experiments of last year it was proved that, as a rule, the normal liquids of the animal body (blood, tissue, juice, &c.) do not contain microzymes either in germ or visible form. It was also proved that in common drinking water and in other watery liquids with which the body is constantly in contact, microzymes, although not distinguishable by the microscope, exist potentially, that is in germ. From these facts, taken in combination with the existence of similar organisms in infective exudation-liquids, the inference is very obvious that, inasmuch as these organisms cannot have originated from the normal tissues or juices, they must have been derived from the external moisture.

This inference would of course at once fall to the ground if it could be shown either that microzymes spring up of themselves, or that the forms which occur in the animal liquids are not specifically identical and organically continuous with those which exist in aqueous media outside. In the absence of any such proof, I am not aware of any objection to the assumption of their external origin, and am quite willing to admit it, provided that it is clearly understood that, even if the extrinsic origin of microzymes were proved, it would afford no ground for concluding that the origin of the contagium itself is also extrinsic. It does not at all follow because these organisms come in from outside that they bring contagium along with them ; for it may be readily admitted that they may serve as carriers of infection from diseased to healthy parts, or from diseased to healthy individuals, and yet be utterly devoid of any power of themselves originating the contagium they convey.

B.—Report of 1875.

In 1872 I had the honour of communicating to the Medical Department of the Privy Council a Report of investigations then made under their direction, on the subject of acute secondary inflammation in animals, the purpose of the inquiry being to throw light on the processes by which the infections which in man are associated with acute diseases of traumatic origin, are conveyed from diseased to healthy persons.

It having been shown by my own observations as well as by those of others, that in the various forms of secondary inflammation in animals, the exudation liquids of ordinary inflammations are always endowed with toxical properties which are not possessed by other animal fluids, and which manifest themselves either in the production of local inflammation in the living tissues with which such liquids are brought into contact, or in the production of acute general disorder consequent on their existence in the circulating blood or in the tissues, it became of importance that the nature of the toxical agent to which these effects are attributable, and the conditions of its action, should if possible be determined.

With this view a series of experiments was made in the Brown Institution at the period already referred to, of which some of the results were reported ; as however no opportunity then offered itself of making them public in the usual way, they were, with the permission of their Lordships, communicated to the Royal Medico-Chirurgical Society and published in the 56th volume of the Transactions of that body. They

were shortly afterwards translated into German and published in the *Wiener medicinische Jahrbücher*.

In the course of these experiments a new and most important fact came to light, namely, that in the transmission of infective inflammation in a series of animals, by inoculation from animal to animal, an *augmentation of infective activity* takes place, which is of such a nature that, whereas at the beginning of the series the effects produced by a given dose of infectious liquid are inconsiderable and transitory, a product is eventually obtained which possesses toxical powers of the most intense virulence. The experiments which led to the discovery of this fact were as follows :—

Experiment I.

On the 18th of March 1872, three and a half minims of dilute *liquor ammoniæ* (which had been previously boiled and cooled) were introduced into the peritonæal cavity of a guinea pig, the instruments used for the purpose being a cannula which had just been subjected to prolonged boiling, and a freshly made glass pipette. On the day following, the animal was killed, and the exudation liquid contained in the peritonæal cavity was immediately injected into the peritonæal cavities of two other guinea pigs, of which one became collapsed soon after the injection, and survived only six hours; the other was killed about 24 hours afterwards. In both animals there was intense peritonitis. In the second guinea pig (which was killed) the fluid exudation was clear and viscid and of a yellow colour ; it was crowded with minute organisms.

On the following day three and a half minims of this fluid were injected into the peritonæal cavities of two other guinea pigs, neither of which survived more than 24 hours. Exudation liquid was collected from one of them in a glass tube just drawn out and cooled, and immediately sealed up hermetically Of this product 18 minims were on the 23rd, *i.e.*, two days after, injected into the peritonæum of a moderate sized dog. Death occurred in six hours. Shortly after the injection the animal became affected with tenesmus, vomiting, and diarrhœa, which speedily subsided into fatal collapse.

Experiment II.

Five minims of liquid derived from an infectively inflamed lymphatic gland of a guinea pig, were injected into the peritonæal cavity of two others on the 16th of March.

In both animals the injection resulted in intense peritonitis, with purulent false membranes on the serous surfaces of the viscera. In one of them, which survived two days, the mesenteric glands were enlarged and softened. On the 18th, five minims of purulent liquid derived from one of these softened mesenteric glands, and charged with organisms, were introduced into the peritonæum of another guinea pig. In this animal the peritonitis was again very intense, and yielded an exudation fluid, which was injected into three others, each receiving six minims, all of which became collapsed shortly after the injection. After death the peritonæal cavity, of which the surface was intensely injected, was found to contain viscid exudation fluid crowded with organisms. The extreme activity of the virulent liquid was further tested by injection to carnivora, namely to four dogs and two cats ; of the former, three received

from seven to twelve minims each in the peritonæum, the fourth by injection into a vein. Death occurred at various periods between four and twelve hours, and was preceded by collapse ushered in by vomiting, tenesmus, and diarrhœa. In the two cats the phenomena were essentially the same, the duration being five hours in the one case and two in the other.

From the above experiments, which with others were tabulated in the Report of 1872, it was ascertained that when in a series of rodent animals and particularly guinea pigs, inflammation of the peritonæum is communicated from one to another, by the injection into the peritonæal cavity of each in its turn, of exudation liquid derived from its predecessor, the process thus transmitted appears to gain in intensity by transmission, so that sooner or later a product is obtained which, when tested by injection into the peritonæum of a carnivorous animal, is found to possess an extreme degree of virulence.

In order to determine under what circumstances this intensification occurs, and to obtain more precise information as to the phenomena during life, and the pathological appearances after death, with which it is associated, I have more recently thought it necessary to make the following experiments, which have also been carried out at the Brown Institution :—

Experiment III.

The form of the experiment is shown in the diagram.

Primary peritonitis was induced on the 3rd of February 1875 by the subcutaneous injection of four cubic centims. of a mixture of nine parts of distilled water with one part of liquor ammoniæ. The liquid was boiled and cooled. Twenty-four hours afterwards a large quantity of subcutaneous exudation liquid was obtained from the moribund animals, of which 1·62 cubic-centims. were injected to the next in the series (No. 2). From No. 2, which died during the following night, peritonæal exudation liquid was injected into the peritonæum of No. 3, the dose being reduced to 0·486 c. c. (= six divisions of the Pravaz syringe used). Similarly No. 4 was infected from No. 3, and No. 5 from No. 4. In each of the three last-mentioned animals the process was extremely rapid, so that it was difficult or impossible to make useful comparisons of their conditions during life; in No. 5, however, it was apparent, that although the dose of infecting liquid was reduced to four divisions, the induced process had reached an extreme degree of intensity, death occurring in four and a half hours after injection. This being the case, we injected on the afternoon of February 8th five divisions of peritonæal liquid of No. 5 into No. 6. On the following morning it was found that the cannula had failed to enter the peritonæum. We therefore withdrew some of the subcutaneous exudation thus produced, and injected it immediately into the peritonæum

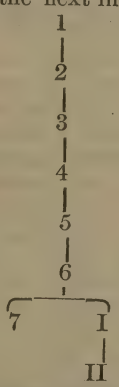


Diagram of Experiment III. The Arabic numerals indicate guinea pigs; the Roman, dogs.

of the same animal. By this expedient we obtained in No. 6, after 10 hours, a sufficient quantity of viscid peritonæal exudation fluid, which we at once recognised as having in all respects the same characters as the extremely virulent fluid with which we had experimented in 1872.

Having thus good reason to believe that we had accomplished our object, we injected two divisions of this liquid to another guinea pig (No. 7), and eight divisions to a dog (No. I.). The former died during the following night, yielding an exudation liquid which was exactly the counterpart of that by which it was produced ; the latter survived for nine hours. From its peritonæum, liquid was obtained immediately after death, and at once injected in similar dose into the peritonæum of another dog (No. II.), which died in seven hours.

It was thus conclusively shown that it is possible to proceed from an inflammation of purely non-infective origin, to the artificial induction of a process of the most intense virulence. The phenomena observed in the several animals used were as follows :—

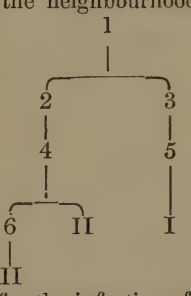
1. In the guinea pigs 3, 4, and 5 the exudation liquids were for the most part muddy, and showed a mere trace of sanguinolent staining. On microscopical examination they were found to contain no blood disks, but numerous pus corpuscles. In No. 3 these corpuscles floated freely and singly in the liquid, but in 4 and 5, where they were in greater numbers, were aggregated in clumps. In all the liquids microphytes were abundant, but they presented different characters ; in three they were mostly rods of various but usually considerable length ; in 4 and 5, rod-forms also occurred in considerable numbers, but they were shorter, (commonly about twice as long as broad), and more minute. In addition to these, the liquids of 4 and 5 contained countless myriads of spheroids (micrococci) which were either free or in masses. It is by these masses of living spheroids that the pus corpuscles are held together so as to form the clumps already mentioned. In all the animals it was observed that the exudation liquid in the pleura—the inflammation of which was of course secondary, *i.e.*, produced by infection from the peritonæum—presented in each case characters which corresponded with those observed in the peritonæum itself.

2. In No. 6, as has been already stated, the point of the cannula unintentionally failed to enter the peritonæum, in consequence of which the injected fluid was diffused in the tissues of the abdominal wall. Sixteen hours after, a swelling existed at the seat of puncture, from which a liquid was withdrawn, and at once transferred to the peritonæal cavity. The resulting peritonæal exudation collected after 10 hours, differed from those previously described in being perfectly colourless, milky, and viscid ; it was found to contain numerous pus corpuscles, which, as in the other exudations, were collected together in clumps, of which the interstitial material consisted of masses of spheroidal organisms. The liquid in which the clumps floated was also crowded with shining spheroids, some of which were isolated, others in dumb-bells or chains. Rod-like bacteria were entirely absent. Every pus corpuscle was itself crowded with spheroids embedded in the substance of its protoplasm. The colourless and viscid exudation liquid which was obtained from the guinea pig No. 7, which was injected with the liquid just described, resembled it in every respect, excepting that in addition to the microscopical clumps, the field was scattered with larger fleecy masses of micrococci also containing pus corpuscles. This liquid was slightly alkaline, and left on evaporation at 100° C. 5·01 per cent. of solid residue. The specific gravity was 1019·3.

3. In order to test the activity of the exudation liquid of No. 6, a black and tan terrier, weighing about 8 lbs., received in the peritonæum, one and a half divisions of it mixed with an equal quantity of half per cent. saline solution. The animal shivered violently an hour after the injection, and had diarrhœa and vomiting soon after. The enteric symptoms attained their greatest violence about four hours after injection, at which time the animal appeared to suffer much from tenesmus; the *sphincter ani* was relaxed, and there were frequent discharges of bloodstained mucus. Death happened eight hours after injection. The maximum of pyrexia was attained during the fourth hour; the highest temperature observed was 41°·2 C.(106°·2 F.), the previous normal being 38°·6 (101°·5 F.). On dissection, the peritonæal cavity was found to contain a muddy sanguinolent liquid; on microscopical examination it was seen to be crowded with large pus corpuscles, all of which were charged with micrococci. Both the pleural and peritonæal surfaces exhibited hæmorrhagic spots, but the pleura in this case contained no exudation. The dog No. II., weighing 9 lbs., received 3·9 cub. centims. of peritonæal liquid from No. I. Two hours after injection there were severe rigors, but scarcely any rise of temperature. In two hours more, the animal was moribund, its temperature having sunk to 35°·3 C. On dissection the peritonæal cavity was found to contain a considerable quantity of blood-coloured viscid fluid; the omentum and mesentery were beset with hæmorrhagic spots. The mucous membrane of the stomach and of the whole intestinal tract was intensely congested, being of a dark crimson colour throughout. Microscopical examination showed the exudation liquid to contain numerous pus corpuscles, all of which were charged with micrococci. Similar organisms also existed free, but not in such crowds as in the colourless viscid exudations of guinea pigs. Notwithstanding the intensely sanguinolent colour of the liquid, it contained scarcely any blood disks.

Experiment IV.

Primary inflammation was produced as in the former case, by the injection into the subcutaneous cellular tissue, of eight-tenths of a cubic centimeter of dilute ammonia. Thirty hours afterwards an abundant exudation had taken place under the skin in the neighbourhood of the seat of injection; there was also exudation fluid in the pleuræ. Of the former, seven divisions were injected into the peritonæal cavity of guinea pig No. 2, and of the latter a similar quantity to No. 3. No. 3 died in four hours; the exudation liquid served for the injection of No. 5. This animal yielded a characteristic colourless viscid liquid which was at once injected into the peritonæum of dog No. I. The dog died in six hours, with intense symptoms. At the same time that No. 5 was infected from 3, 4 was infected from 2, affording in its turn liquid for the infection of two other animals, a dog (No. II.) and a guinea pig (No. 6.)



In these eight animals, the symptoms and pathological appearances were as follows:

The animal primarily affected survived injection 30 hours. The subcutaneous liquid was slightly alkaline: its specific gravity was 1017·4 and it left on evaporation at 100° C. 5·3 per cent. of solid residue. It contained very few blood disks, and relatively few pus cor-

puscles, but it was crowded with rod-like filaments of various lengths, along with spheroids, chains, and dumb-bells, in considerable numbers, and a few crystals of ammonio-magnesic phosphate. The exudation liquid collected from the pleuræ contained no filamentous organisms, (bacteria proper) but innumerable spheroids, and a few short chains and dumb-bells: there were also a few pus cells, in all of which the cell substance was beset with spheroids.

Guinea pig No. 3, which was injected at 12 o'clock with the pleural liquid just described, died about 4 the same afternoon. The peritonæal exudation was pale-coloured and viscid. It contained flakes or shreds, visible to the naked eye, and was crowded with free spheroids, dumb-bells, and chains, amongst which no rods or filaments could be distinguished. It also contained pus corpuscles, some of which were isolated, others in clumps. In these clumps, as well as in the larger shreds already referred to, the corpuscles were held together by a mass of spheroidal particles.

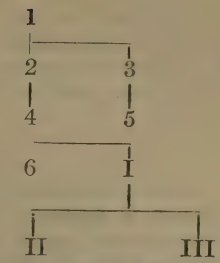
Guinea pig No. 5, which was injected at 5 o'clock with four divisions of the peritonæal liquid of No. 3, was already moribund at 9 in the evening. On the following morning the exudation liquid contained in its peritonæal cavity was collected. It was pale, viscid, and crowded with organisms, which corresponded in character to those found in the exudation liquid of No. 3. It was used to inject dog No. I.

Dog No. I., weighing about forty pounds, received fifteen divisions of the liquid of No. 5. The injection was made at 11.30 a.m., and death occurred at 5 p.m., the symptoms being those already described as characteristic of intense infection. On opening the abdominal cavity after death, the peritonæum was found to be intensely hyperæmic, the mesenteric veins being distended with blood, and the surface of the mesentery as well as that of the omentum scattered with numerous hæmorrhagic spots. The mucous surface of the stomach and small intestines was so intensely congested, that it was of a uniform dark red colour throughout. It was covered with a layer of bloodstained mucus, which material constituted the only contents of the stomach and intestine. The peritonæal exudation liquid contained 15·08 per cent. of solids, its specific gravity being 1041. It was slightly alkaline, and did not coagulate spontaneously even when placed in the warm chamber at 32° C.; on the addition of serum, however, it became flaky. Notwithstanding its intensely sanguinolent colour, it was found on microscopical examination to contain scarcely a single blood disk; in microscopical preparations, crystals of hæmoglobin were found in abundance near the edges of the cover glass; a few drops of the liquid allowed to evaporate in a watch glass also crystallized readily. Pus corpuscles and endothelial elements, either isolated or in clumps, existed in great numbers; the former contained innumerable spheroids embedded in their substance; the liquid was charged with the usual forms, particularly spheroids and dumb-bells of extreme minuteness.

The dog No. II (weight 10 pounds), which was smaller than the one last referred to, and received a similar dose of exudation from the peritonæum of guinea pig No. 4, exhibited similar symptoms, but recovered. The guinea pig injected at the same time (Febr. 20), and with the same liquid, survived seven hours. The colourless viscid exudation contained in its peritonæum having been collected in a glass tube and sealed hermetically, 10 divisions of it were subsequently (Febr. 23) employed to infect dog No. II a second time, the animal having completely recovered. His temperature rose in consequence only eight-tenths of a degree in three hours, and then declined. He recovered without further symptoms.

Experiment V.

On the 22nd February 1875, eight divisions of boiled and cooled solution of ammonia, containing before boiling one part in ten of liquor ammoniæ, were injected subcutaneously to a guinea pig (No. 1). The animal survived 21 hours, and afforded material for the infection of two others, one of which (No. 3) received exudation liquid collected from the peritonæal cavity; the other (No. 2) the liquid effused subcutaneously in the neighbourhood of the puncture. From the latter the guinea pig No 4 was infected, and from that the guinea pig No. 6 and the dog No. I. which finally served to infect two others; from the former, liquid was collected for the injection of No. 5.



In guinea pig No. 1 the quantity of subcutaneous liquid was relatively very small, and differed from those previously used in the small number of pus corpuscles it contained. The peritonæal and pleural liquids exhibited the usual appearances, and contained rods, spheroids, and dumb-bells in great numbers. In No. 2 the period of survival could not be determined, but was probably about eight hours. The viscid exudation liquid from the peritonæum contained, along with the usual anatomical elements, spheroids, dumb-bells, and short chains, which were either isolated or in small masses. None of the liquids coagulated. In guinea pigs Nos. 3 and 6 the peritonæal liquids presented the usual characters, the period of survival being in each case about seven hours. In both the blood was carefully examined, and found to contain spheroids similar to those of the exudation liquids.

The dog, No. I., weighing 15 lbs., which received in its peritonæum 3·9 cubic centims. of the same liquid which was used for the infection of No. 6, survived seven hours, exhibiting the same symptoms as in the other cases. The appearances observed on dissection, were also similar to those already fully described in Exp. IV., but by no means so intense. Both the peritonæal liquid and that obtained from the secondarily inflamed pleuræ were crowded with the organisms usually observed, the presence of which could also be detected in the blood.

From this animal two others were infected, but by different channels. Dog No. II., weighing about 6 lbs., received in the peritonæum four divisions (*i.e.* $\frac{1}{10}$ of the previous dose) of peritonæal exudation from No. I., and died in 14 hours, with the usual symptoms and post-mortem appearances. In dog No. III. 5 cubic centimeters of peritonæal exudation, previously filtered through paper, were injected on the 1st of March into the circulation by the tibial vein. The immediate effect produced by the injection was very inconsiderable, the maximum rise of temperature amounting only to 1°·6 C., *i.e.*, not more than is often produced by the injection of a similar quantity of distilled water; but the following morning the animal refused food and was apparently in pain. On the 3rd (the day after) he was still suffering; when an attempt was made to examine him, he struggled so violently, that it was found impossible to observe his temperature. Next morning he was killed, and the body immediately afterwards dissected.

On removing the integument covering the thorax, a quantity of pale yellowish exudation was found infiltrating the tissue in the neighbourhood of the articulations of the fourth and fifth ribs with their cartilages, and extending to the intermuscular spaces to a short distance. In pursuing the examination, similar cellular infiltrations were found in

other parts, particularly subcutaneous tissue about the left elbow joint, and around the left tarsus. The internal viscera were apparently healthy. The pleural and peritonæal cavities were sparingly studded with hæmorrhagic spots, and contained small quantities of liquid which on microscopical examination, was found to contain the usual organisms.

Conclusions.

From the preceding experiments we learn that whenever an inflammation is produced in a guinea pig, of such a nature as to result in the exudation of liquid, either in the cellular tissues or into a serous cavity, that exudation liquid possesses an infective property which, for the purpose of distinguishing it from the properties of other morbid contagia as well as from that which manifests itself in the production of fever, may be designated *phlogogenic*, the property in question consisting in this, that if such a liquid is injected into a second animal of the same species, *it produces an inflammation which is similar in character to that of which it is itself the product.* Inflammations so produced we may conveniently term "transmitted inflammations," reserving the expression "secondary inflammations" for those which originate in the same organism at a distance from any traumatic (primary) inflammation, by self infection.

We have seen it to be the result of observation that the intensity of any transmitted inflammation is dependent on the intensity of the inflammatory process by which it was produced, or, in other words, that those transmitted inflammations are most intense which are begotten of the most intense antecedents. We have also seen that if a process of inflammation is transmitted in a series of animals from one to another in such a way that each is infected by the introduction into its body of exudation liquid derived from its predecessor, the transmitted process become on the whole more intense towards ths end of the series. But it is not true, as I was at first inclined to suppose, that this increase of intensity by transmission progresses in a gradual or regular manner. I have learnt this by direct observation. All the experiments, and particularly the third and fourth, which were expressly contrived for the purpose of showing such gradual intensification, distinctly indicate that the augmentation does not take place by successive steps but *per saltum.*

How this happens may, I think, be readily understood if it be borne in mind, that the intensity of a transmitted inflammation is determined not merely by that of its immediate antecedent, or, in other words, by the virulence of the transmitted liquid, but also by the condition of the individual animal which is the subject of it. If the augmentation were a gradual one, we should express the whole truth in comparing it to a process of cultivation, that is, in supposing that the phlogogenic agent *itself*, by passing from the body of one animal to that of another, undergoes a gradual development of its infective power, in a manner comparable to that in which we imagine a plant to be modified gradually by being planted in a soil different from that to which it is naturally habituated. The fact that this is not the case, but that in a series of transmissions the intensification of virulence appears, as it were, *per saltum*, can have no other explanation than the one already suggested, namely, that the conditions belonging to the infected individual are no less efficacious than those which belong to the material transmitted.

This being admitted, there are two such conditions as regards the guinea pig to which importance is to be attributed, viz., susceptibility and endurance. As regards susceptibility, it is so nearly equal in all

cases, that its influence becomes inappreciable; for our observations show distinctly, that inflammations which are the products of not more than two or three transmissions, may in some cases present the characteristics of extreme intensity. But in respect of endurance there is no such uniformity; all guinea pigs are in the highest degree prone to infection, but all are by no means equally capable of resisting its effects. Many succumb before the process has had time to culminate, and for this reason yield products of an inferior degree of virulence. The most active products are yielded by animals which have *longest* resisted the *most intense* process; so that if I were asked by what method a phlogogenic virus of great activity could with most certainty be obtained, I should say, by first injecting a product of not less than two transmissions to a sufficient number of guinea pigs, and then selecting as a source of virus that which held out the longest.

The fact that in the guinea pig the transmitted inflammatory process may arrive *per saltum* at its highest degree of intensity, even when the infecting liquid is the product of only two transmissions, renders that animal unfit to serve as a criterion, or quantitative test, of any excepting the lower degrees of virulence, just as a spring balance which is stretched nearly to its utmost when loaded to a few ounces, would be of no use in estimating the weight of an object weighing as many pounds. It is for this reason that we have recourse to a standard of less susceptibility.

Such a test we have in the dog, for the organism of the dog appears to be as averse from infection as that of the guinea pig is prone to it. In this respect its condition is probably very near that of man when in health, for which reason the dog is a better standard of comparison than the rodent. Both, however, have their value, for in certain states of health the susceptibility of the human organism, normally intermediate between that of the rodent and that of the carnivora, appears to be enormously increased.

In the dog, as I have ascertained by a sufficient number of experiments not here stated, the injection of a cubic centimeter of primary exudation liquid, *i.e.*, of liquid produced directly by the injection of ammonia or of solution of iodine into the peritonæum, produces no appreciable effect—not because a liquid of this kind is free from infectiveness, for as we have already seen, it acts powerfully on the guinea pig, but because the living tissues of the dog have resistance enough to counteract its influence. It is not until we deal with exudation products of the highest degree of virulence, that we obtain those decisive effects of which I have given instances in the preceding paragraphs.

In employing the dog as a test of the infective activity of an exudation liquid, whether derived from another animal of the same species or from a rodent, it is important not merely to determine by experiment the smallest dose of the agent or material to be investigated, which is capable of producing fatal infection, but to endeavour to measure the intensity of the action in each case, by the pathological appearances found after death and by the symptoms during life. As regards the latter, the means which is of most use in enabling us to judge of the intensity of an infective process, is the observation of the changes of bodily temperature which follow infection. Of these, three principal varieties have presented themselves in the course of our experiments. In what may be called the normal case, in which a liquid of moderate intensity is used, the injection is followed, after a very short period of latency, by violent rigors attended by rapid rise of temperature, during and after which the animal has more or less of vomiting and tenesmus, and discharges mucous or sanguinolent evacuations. Secondly, we have cases

representing the smallest appreciable degree of infective action, in which the rise of temperature, inconsiderable as it is, is the only sign of constitutional disturbance; and lastly, those in which the elevation of temperature is also slight, but for a very different reason. Of these last we have a good example in Experiment IV. In this animal the rigors commenced within two hours after the injection, but the bodily temperature, which had previously maintained itself a fraction of a degree above the normal, fell rapidly after the close of the third hour, until the animal died collapsed.

These phenomena are readily enough understood if attention is paid to the relation between the temperature changes, and the condition of the animal. What may be called the normal effect of the introduction of an infective agent into the organism, is to produce rigors with coincident and consequent pyrexia, attaining its maximum in three or four hours, and then subsiding. But this standard may be departed from either in the direction of excess or in that of defect. In the former case, when the absence of pyrexia is due to excess of infective action, it denotes not that the agency which in the less severe cases produces pyrexia is absent or even in abeyance, but that its influence is counteracted by others, and particularly by those which tend to general weakening of systemic life and diminished circulation.

Notwithstanding the apparently intimate relation between the elevation of temperature and infective action of the kind we are now engaged in studying, it is not by any means to be taken for granted that this elevation results directly from the introduction of the infective agent into the circulating blood. There is, on the contrary reason for believing that here, as in the case of the specific infections, the pyrexia is rather a secondary result of processes having their seat in the inflamed parts, than of a direct absorption into the blood of phlogogenic virus; for we have repeatedly observed, that even when considerable doses of virulent liquids are injected directly into the blood-stream, the resulting fever is often very inconsiderable. Hence we conclude, that although in all infective inflammations the presence of a fever-producing agent is plainly indicated, it would be a mistake to regard the phlogogenic and the pyrogenic actions as identical in their nature.

In conclusion I would refer to the differences which present themselves between infective liquids of different intensities. These differences are so characteristic, that the practised observer has no difficulty in recognizing a highly infective product by its physical and microscopical characters, even if unacquainted with the pathological conditions under which it was produced. The highly infective serous exudation products of guinea pigs, have always a high specific gravity, fail to coagulate, and possess a viscidity so peculiar that it alone would serve as a characteristic. They are further distinguished by the presence of the spheroids and dumb-bells so often referred to, either isolated in the liquid, collected in colonies or cloud-like masses, or embedded in the cell substance of pus corpuscles. In the dog the same characters present themselves, with this important difference, which I am quite unable to account for,—that, as the reader must have noticed, the liquids are almost always more or less blood-coloured, whereas in the guinea pig they are always colourless. The staining is very often so intense that it might be supposed to arise from extravasation. There is, however, no difficulty in proving the contrary, for on microscopical examination it is found to contain absolutely no blood disks, and when examined by the naked eye with transmitted light (as, for instance, when enclosed between two glass plates held between the eye and a window) it is seen

to be transparent. The blood-colouring matter, therefore which is present, is not in its natural condition, but in a state similar to that in which it exists in blood which has been several times frozen and thawed, a fact of which proof can be readily obtained by slowly evaporating a small quantity of the exudation liquid in a watch glass. As evaporation proceeds, hæmoglobin crystallizes.

In conclusion, I think it desirable to repeat what I have often had occasion to insist on elsewhere, that the presence of characteristic organic forms in infective liquids, affords *in itself* no conclusive evidence that these bodies are themselves the cause of the infectiveness. If we inferred from the constancy of their characteristics and from their invariable presence, that they are the *agents* which produce the pathological results, we might be as seriously in error as those are who maintain, in the face of all the investigations relating to the subject made during the last few years, that they are without pathological significance. There is nothing in nature, and particularly in organic nature, without significance, nor ought it in the slightest degree to diminish the interest which we take in any phenomenon, that we are unacquainted with its relation to the other phenomena with which we find it associated. If these infinitely minute organisms are present in every intensely infective inflammation, we may be quite sure that they stand in important relation to the morbid process.

App. No. 3.

On Enteric or Typhoid Fever, by Dr. Klein.

No. 3.—Dr. Klein's Report on the Intimate Anatomical Changes in Enteric or Typhoid Fever.

Introduction.

The anatomical changes of the intestine, the mesenteric glands, and spleen in enteric fever, have been the subject of much careful study, as the works of Louis, Chomel, Gerhard, Jenner, Stewart, Rokitansky, and others evince. Especially since the most elaborate research on this subject by Hoffmann,* there seems to be left little to be added to the gross pathological anatomy of those organs.

This is not, however, the case with the minute anatomy, for although from the works of Grohe, Billroth, Rindfleisch, Hoffmann and others, it might appear as if we understood all the histological characters of the lymphatic apparatus of the intestinal canal in the different stages of that disease, I shall show that a number of important changes, regarding the minute anatomy of the solitary and agminated glands of the ileum and of the mesenteric glands and spleen, have been left altogether unnoticed by previous observers.

The present research was undertaken with a special view to inquire whether the supposition—based on clinical observation and chiefly on etiological data—that the contagion of enteric fever is a living organism, probably, like that of smallpox, of the nature of a minute vegetable fungus, can be proved by anatomical observation to be a fact; that is to say, whether it can be shown not only that peculiar organisms are present in the intestine and the diseased parts, but that there is a special relation between the progressive changes of the latter and these organisms, similar to what has been shown to be the case in the smallpox of sheep. I have, therefore, devoted a great deal of attention to the microscopical changes of the mucous membrane and the lymphatic follicles of the ileum, in order to see whether special organisms can be detected in these parts, and what relation they bear to them.

Some time ago I had the opportunity of pointing out in a preliminary publication † the presence of peculiar bodies, of the nature of minute vegetable organisms, in the mucous membrane of the intestine in early stages of enteric fever; since then I have been able to satisfy myself that it is highly probable that the presence of these organisms bears an important relation to the diseased parts, being perhaps the chief of the causes of the death—ulceration—of the lymphatic follicles.

Investigations of this kind can, for obvious reasons, be only satisfactorily carried out when the material to be subjected to microscopic examination can be obtained in a sufficiently fresh condition, *i.e.*, immediately or very soon after death. This, however, has been—I trust a change for the better will take place some day—accomplished with greater difficulty than I expected, owing to the regulation in many of the hospitals in London that post-mortem examinations can be made only after the lapse of a certain time, I believe at least 12 hours. Now, it is necessary to bear in mind that the epithelium of the mucous membrane

* Untersuchungen über die patholog. anatom. Veränderungen der Organe beim Abdominaltyphus. Leipzig, 1869.

† Centralblatt, September 1874.

of the intestine, the Lieberkühn's follicles, the tissue of the villi, and in general the superficial parts of the mucosa, are very liable to undergo changes in consequence of decomposition setting in soon after death, even in healthy intestine, and that these changes are much more rapid in an intestine that has been already during life the seat of disintegration, as is the case in enteric fever. The reader will soon have the opportunity of seeing that the examination of the superficial parts of the mucosa obtained in good condition is of extreme value for the research.

If it had not been for the great kindness of Dr. P. H. Mackellar, physician to the Fever Hospital at Stockwell, to whom I have to tender my best thanks, I should not have been able to follow out some of the most important points of this investigation. I have also to thank Dr. Creighton, formerly medical registrar of Charing Cross Hospital, and Dr. Mahomed, formerly physician of the Fever Hospital at Islington, for their kind assistance in furnishing me with material of some interesting cases, to be mentioned hereafter.

All experienced pathologists regard enteric fever as a disease due to a specific poison. As Liebermeister* so impressively argues, it ranks among those infective diseases which are of a contagio-miasmatic character. Dr. Budd,† Professor Biermer,‡ and Professor Liebermeister have, from their own observations and from those of others, put together, with considerable clearness and force, the theoretical considerations and actual facts which lead to the conclusion that the contagion of enteric fever is due to a specific and living organism, which, when transmitted from a diseased to a healthy individual, produces the same disease in the latter. It is forcibly argued by these and former observers, that the chief, and perhaps the only vehicles of the poison, are the ejecta of the bowels of the infected person; and that the contagium contained in these ejecta is introduced into a new individual, either in the solid or (apparently) gaseous condition, that is to say in inspiration, in food, or in drink. Liebermeister thinks that the contagium of enteric fever cannot produce infection, *i.e.*, that it is inactive, immediately after it is discharged from the diseased bowels, and has to go through a certain process—probably some kind of development—before it again assumes its active condition. This agrees with the general observations of many physicians, so thoroughly discussed by Dr. Murchison. § Even when the germs in their active condition enter a healthy organism which has not yet been subject to the disease, they do not manifest their obnoxious effect at once, but remain for some time innocuous, or, more properly speaking, latent. This represents the time of incubation. During this time, as Liebermeister very ably argues, they are probably hidden in certain organs—in enteric fever in the lymphatic apparatus of the intestine—where they ripen towards their active condition, and pass perhaps through another stage of development.

Looking at the great number of etiological data which support the theory that the contagium of enteric fever is a living organism, the above explanation of incubation is almost a necessary conclusion; but I would rather express it thus: this being the only possible way of explaining the incubation, the theory that contagium is organised is prima facie thoroughly justified.

The attempt to investigate the character of the contagium of enteric ever by communicating the disease to the lower animals, has, as far as I am

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* See Ziemssen's Encyclopædia of Medicine; Enteric fever.

† Typhoid fever; its Nature, Mode of spreading, and Prevention. London, 1873.

‡ Sammlung klinischer Vorträge; herausgegeben von Richard Volkmann, No. 53, p. 411.

§ Treatise on Continued Fevers; second edition. London, 1873.

aware, completely failed, and the hope of advancing our knowledge of this subject by means of experiments, similar to those successfully undertaken with vaccine lymph and the lymph of smallpox, must for obvious reasons be for the present abandoned. Thus we are left to depend on microscopic examination. As far as I know, nothing has been done in this respect hitherto, except some very vague assertions about the presence of bacteria in the blood of patients suffering from enteric fever; even in the systematic works on the minute anatomy of this disease no mention is made of the presence of any specific materies morbi. The subject has in general received but little attention.

Hallier, in his well-known investigation on the fungus contagium of the different acute infectious diseases, found also for typhus and typhoid fever specific forms. *

1. *Preliminary Investigations.*

I commenced my investigations with the examination of the fresh stools of patients suffering from diarrhœa in the first three weeks of enteric fever; the stools were of the well-known characters, being ochre-coloured, thin, composed of a clear fluid in which were suspended pale yellowish smaller and larger flakes and lumps. Of the fresh stools ½ to 4 drachms were placed in a bottle containing about 4 ounces of water. Several samples from the same patient were thus collected during several days and then examined; the examination of each sample was extended over a period varying from three days to three weeks.

This is what I find in the discharges: large masses of an amorphous more or less coarsely granular or homogeneous-looking, yellowish-brownish material; masses of fatty substance, and finally irregular masses of very transparent substance showing in many places something like residues of nuclei cells and fibres. The objects last mentioned I need hardly say are found only in the later stage of the disease, in and after the third week, viz., when ulceration has already commenced. These masses form the gros of the solid parts.

Besides these, there are invariably found numerous isolated bacteria termo (apparently resting), which are the more numerous the later the examination is made. At the same time actively moving bacterium termo (due to putrid decomposition) make their appearance. As we shall presently hear, if access of air is not prevented, they soon increase to such an extent, that the material becomes swarming with them. In the recent period the material, however, contains—and sometimes this is a strikingly prevalent feature—isolated and also spherical micrococci of a very characteristic appearance.

I will give in the following paragraphs a few examples:

a. 14th December 1874. Examined fresh stools (macerated in water) of enteric patient—third week's duration: numerous spherical lumps of different sizes of a more or less dark yellowish-brownish colour; the matrix of these lumps —a soft, gelatinous, transparent substance (easily flattened out by pressure into irregular shapes)—filled with uniform spherical micrococci. After 24 hours' incubation (39° C.) of a small portion of the material, the number of these spherical lumps increased to a great extent; there were also large continuous masses of them.

In the fresh samples, as well as in those that have been kept for 24 hours in the incubator, isolated micrococci were contained, besides dumb-bells and chains or necklaces of them; the last-named forms were much more numerous

* See Murchison, Treatise on Continued Fevers, p. 9.

in the specimens that had been exposed to the constant temperature. [See Fig. I. a. b. and c. and the explanation.]

During the following 8 or 10 days the number of moving bacteria termo increased to an enormous extent—formation of a pellicle on the surface—in those samples in which the access of air was not excluded (owing to lifting the stopper of the bottle when preparing microscopical specimens), whereas in those bottles which remained closed the pellicle covering the surface, as well as the fluid, contained no moving bacteria termo, but thick short rods in a resting condition; having a shallower or deeper constriction in the middle, they resembled more or less dumb-bells; there were very numerous spherical examples among them. The pellicle especially showed these forms very distinctly; and it could be easily ascertained that the elements are far larger, *i.e.*, thicker than in the pellicle of those samples to which the air had access, and in particular it could be proved that the micrococci are derived from the rods above named. See Fig. I. d.

The samples contained at this time, as well as later, numerous micrococci like those found in the fresh specimens. They could be easily distinguished from the last-named forms of micrococci by being smaller and much more highly refractive. (See Fig. I. e.)

It remains to be added that in those samples to which the access of air was free, the original spherical yellowish-brown zoogloea of micrococci, described above, gradually disappeared as the moving bacteria termo increased.

b. 26th December 1874. Several samples of stools of a recent case of enteric fever were collected at several subsequent days and treated as before. They invariably contained numerous bright highly-refractive spherical large micrococci; their diameter about one-third of a coloured blood corpuscle, they show slight differences in size; they are isolated, or in dumb-bells, or in small groups. Many of them show a small dark speck at one point of the periphery. (See Fig. I. f.)

In the samples to which the air was allowed free access, moving bacteria appeared in great numbers, but the bright micrococci above mentioned remained very numerous even after many days. Those samples, however, which remained closed, when examined after six days, contained a great number of rod-like structures—larger than the ordinary moving bacterium termo—from which micrococci similar to the bright ones could be traced to originate. Not only was there uniformity in their substance and thickness, but there were many intermediate forms between the two, viz., from rods with more or less deep transverse constrictions, up to distinct dumb-bells. Until the 9th of the following month the number of the bright large micrococci was very considerable.

Besides these, I examined several other cases in which, in the fresh condition, there were numerous bright micrococci, perfectly identical with those just described.

For the present I must be satisfied with merely recording certain facts, but we shall return to these organisms in a later chapter, when we come to discuss the presence of micrococci in the tissue of the intestinal mucous membrane.

2. *Attempts to communicate Enteric Fever to animals.*

Having carefully studied the samples of stools of cases of enteric fever which I was possessed of, I tried to reproduce the disease in animals by mixing with their food small portions of that material, bearing in mind that according to the notion of the most experienced observers who have investigated the etiology of enteric fever, the contagium is contained in the alvine dejecta of patients suffering from that disease. I chose monkeys and white mice as the animals on which to experiment; monkeys for the reason that, being nearest to man, they are more likely to take the disease than other animals of which I had already had some experience, having previously tried guinea pigs, rabbits, dogs, and cats without success; and white mice for the reason that they have

been successfully used by Professor Thiersch and Dr. Sanderson for producing something like cholera by feeding them on cholera-stools. With regard to the last-named animal, I have been unsuccesssful, as far as my experiments go, but as they were only few in number, I am not inclined to regard this negative result as definitely settled, but think of repeating them on some future occasion. Likewise I am sorry to state that the experiments on monkeys failed completely. I will describe the particulars of the following experiments :—On the 12th of January, 1875, small quantities of alvine discharge obtained from a patient in the third week of enteric fever, which had been kept macerating in water in a bottle since the 14th December, were mixed with milk and given to two perfectly healthy monkeys to drink ; each of them received about $\frac{1}{2}$ a drachm of the typhoid water, *i.e.*, the alvine discharge macerated in water. They took the milk mixture without the slightest hesitation. The rectum temperature of the animals was taken before the feeding, it was a little above 39° C. As neither of them showed the slightest disturbance of health during the next seven days, *i.e.*, until the 19th January, they were again fed on that day with a mixture of milk and typhoid water, but this time the latter was used fresh, *i.e.*, within 24 hours of its having been obtained. The material was from a patient in the end of the second week of the disease. On the 24th of January both animals seemed to take less food ; one monkey had more copious alvine discharges than usual ; the discharges, however, were firm. The temperature of the same animal was nearly 0·5° C. above its normal, the animal being however very excited. Two days later *i.e.*, the 26th, both monkeys were again all right, and remained as bright as ever during the following days. The cause of this short indisposition can hardly be said to be attributable to the experiment, as it was most probably due to indigestion, the animal having rather over-eaten itself the previous day.

To see whether feeding on typhoid discharges would have the desired effect, if the alimentary canal of the animal had first been made diseased, *e.g.*, by producing a strong intestinal catarrh, about half a grain of elaterium was administered to each of the monkeys formerly used, and likewise to a third on the 1st of February. The medicine was distributed in a small quantity of milk, and as the animals refused to take it willingly, it had to be poured down their throats. It produced, however, no effect, and therefore on the 3rd of February each received six grains of Barbadoes aloes in the same manner as the elaterium. The next day two of them had very bad diarrhœa, the discharges being copious and very thin. These two were therefore fed on a mixture of milk and typhoid water which had been kept in a bottle for 15 days. (*See* experiment on 19th January.) The monkeys were again all right on the 6th, and remained so during the following week.

A last experiment was tried to see whether, under the same conditions as before, viz., the alimentary canal being first brought into a catarrhal condition, feeding on fresh typhoid material would have any effect. All three monkeys were given on the 13th of February three drops of croton oil each. The next day all three had very severe diarrhœa. Fresh typhoid water mixed with milk was then administered to them, the typhoid material having been obtained about 36 hours previously from a recent case. Besides this they were fed a second time on typhoid water on the 17th, the material having been obtained this time 12 hours previously, from the same case as before. I need hardly say that no effect whatever ensued.

3. *Material for Anatomical Examination.*

The material used for anatomical examination was, as as has been already mentioned, ileum, mesenteric glands, and spleen; it was invariably

prepared in the following manner :—Small pieces of intestine, cut out as soon as possible after death (see below), were cut open, washed in bichromate of potash or very dilute chromic acid by moving it gently to and fro, and then placed in a large quantity of one sixth per cent. chromic acid. After 8 to 12 days they were transferred to methylated spirit, and after several days more were used for sections, which were prepared in the ordinary way.

The mesenteric glands were cut out, isolated, hardened in one sixth per cent. chromic acid, and then treated like the intestine ; and, finally, the spleen was prepared by removing small bits about the size of one square inch, hardening them, and treating them in the manner just stated. I have examined material obtained from 16 cases of different stages. Amongst these only seven are worth mentioning specially, as they have yielded special results to be pointed out hereafter. The other cases were of value for general instruction and for confirming some points of minor importance.

The following are the cases worth detailing :—

Case I.—(Case No. 3 of my series). A girl æt. 7. Admitted into the Fever Hospital at Stockwell, December 1st, 1873 ; died on the 3rd of December. Dr. Mackellar writes to me : "The history given by the mother and father was "that she was perfectly well until the 26th November, when she fell in the "street and hurt her head. She seemed well on the morning of the 27th, but "that evening complained of headache. On the 30th she became delirious. "On admission she was quite delirious, screaming loudly, not very conscious. "Much bronchitic tremor in chest. She continued in about the same state "till 8 a.m. of the 2nd, when she became violently convulsed, with rigidity "of limbs, which continued until death—about 17 hours afterwards. All "that time pulse was only an extremely rapid and feeble flutter, respiration "also very rapid and noisy; pupils widely dilated, but no apparent vision. "Temperatures observed were :—

"2nd December, noon, 39·4°C; 10.30 p.m., 41·8°.
"3rd „ 1 a.m., 41·2°.

"No tympanitis, diarrhœa, nor enteric spots."

The patient had not taken any medicine. The friends (Irish) were very clamorous about the remains, so that only a piece of ileum could be obtained. Dr. Mackellar did not regard the case as enteric. On examining the intestine, however, I found in the lower part of the ileum the mucous membrane containing very numerous pale papules projecting over the general surface ; they were in size between a large pin's head and a hemp-seed and larger, their interior being a yellowish-white material. Besides these there was one large Peyer's patch, very conspicuously swollen, and one distinct ulcer, with the slough loosely attached to it. The lower part of the ileum presented precisely the appearance of those rare early cases of enteric fever, in which is observed above the ileocoecal valve a very characteristic eruption of what appears to be swollen solitary follicles,* to which Petit and Serres give the name of "la forme boutonneuse." The microscopical examination further proved that there were very numerous Peyer's glands, which, although they appeared only slightly swollen when viewed with the naked eye, were found to have increased extremely in breadth. Apart from the microscopical examination which showed that many of these papules were due to swollen lymphatic follicles, the presence of a distinct and characteristic typhoid ulcer and of swollen Peyer's glands proved that the case was one of enteric fever ; I am not aware that such lesions occur in any other disease, say meningitis or tuberculosis. Thus death ensued in this case after six days' duration of the fever. The early appearance of an ulcer does not seem to me very extraordinary, considering that the whole character of the case was one of rapid progression ; and besides, Dr. Murchison mentions † a case where at the end of seven days a distinct ulcer could be detected.

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* See Murchison, l. c., p. 613, 16 ; and Dr. Budd, l. c., p. 49, plate No. 2.
† l. c., p. 550.

Case II. (Case No. 4 of my series).—Male, æt. 28. Was said to have been well on the 23rd of November, 1873; headache on the 24th; took to bed on 25th; was admitted into the Fever Hospital at Stockwell on 2nd December; and died on the morning of the 6th December, *i.e.*, after 11 days. He was very delirious and restless most of the time, and often refused nourishment. No diarrhœa nor enteric spots; exceedingly emaciated and feeble. Post-mortem examination 16 hours after death. The lower part of the ileum contained circular, oblong, and irregular-shaped patches raised distinctly over the general surface of the mucous membrane; their diameter very considerable, occasionally 2 to 3 inches. The microscopical examination showed that these patches were due to confluence of neighbouring Peyer's glands, which had encroached on the surrounding mucosa propria. At the same time they were found to extend to a considerable depth towards the external serous covering of the intestine, the whole sub-mucous tissue and also partially the tissue extending between the bundles of the circular muscular coat being transformed into lymphatic tissue. No ulcers could be detected. Mesenteric glands swollen, from the size of a pea to a hazel nut, medullary on section; contain a few yellowish rather firm spots. Spleen enlarged, its substance soft, and of a deep purple colour.

Case III. (Case No. 6 of my series).—Lad, æt. 18. Was said to have been quite well on the 29th of November; vomited and shivered on the 30th; on the 1st December left off working (stationer's porter); took to bed on the 2nd; diarrhœa set in on the 8th; was admitted into the Fever Hospital at Stockwell on the 11th; and died on the 16th, *i.e.*, the 16th or 17th day of the illness. Post-mortem examination seven hours after death. Intense purulent peritonitis, due to perforation of an ulcer in the lower part of ileum. Mucous membrane of ileum in general swollen, and very succulent. Not very much injected. Very few ulcers, chiefly around the one that perforated. Only few patches, raised slightly over the general surface of the mucous membrane. Spleen slightly enlarged.

Case IV. (Case No. 7 of my series).—Lad, æt. 18. Was said to have been well on the 24th of November; headache on the 25th; took to bed on the 8th of December; admitted into the Fever Hospital at Stockwell on the 15th; no diarrhœa before admission, but considerable after; very delirious, great prostration; death on the 23rd December, *i.e.*, after 27 days. Post-mortem examination seven hours after death. Ileum of typical appearance; numerous ulcers. Spleen enlarged, capsule very much wrinkled, the spleen substance soft and flabby and of dark red colour.

Case V. (Case No. 10 of my series).—S. H., girl, æt. 16. Admitted into Charing Cross Hospital on October 12th, 1874, under the care of Dr. Green, in an advanced condition of fever. History unknown. On the day following the admission a number of rose-coloured spots appeared on the abdomen; from this, and from the very characteristic temperature-curve, the duration of the disease could be said to be about 12 or 13 days. Diarrhœa. Since 16th delirious, refused to take food. Died October 17th, *i.e.*, about 17th or 18th day. Shortly before death, acute pneumonia.

Post-mortem examination 12 to 13 hours after death.

I extract from the notes of Dr. Creighton, to whose kindness I am indebted for the description and the material of this case, the following:—Spleen firm, cut surface shining; greatly enlarged, its capsule tense without puckerings. Mesenteric glands greatly enlarged, some of them as large as a pigeon's egg. On section they presented a somewhat mottled red and grey medullary aspect. Intestines in situ much congested in the right iliac fossa. The external surface of the most dependent parts was covered with a distinct layer of fibrinous deposit (peritonitis).

On opening the intestines the duodenum and jejunum showed nothing unusual. About the middle of the ileum the traces of congestion began, and several Peyer's patches were prominent, about a line or so above the level of the surface. Proceeding downwards, several solitary follicles were encountered, in which the ulcerative process was in an early stage. Towards the coecal end there were Peyer's patches, and solitary follicles well advanced in the ulcerative process. In the cœcum also were several ulcerated solitary follicles. Thus the ileum contained solitary and agminated follicles in almost all stages of the process.

Case VI. (Case No. 11 of my series).—R. I. G., Male, æt. 40. Admitted into the Fever Hospital at Islington on January 19th, 1875, under the care of Dr. Mahomed. Too ill (unconscious) to give any account of himself. From his friends it could be gathered that he was at his work until two days before admission; had been, however, feeling unwell for some time previously. Died on January 27th.

Post-mortem examination about an hour after death. Extremely intense purulent peritonitis. The middle part of the ileum was perforated in several places, in which there was adhesion between it and the omentum and other parts of the intestine. At one place a perforation was of such a kind that a fistula was formed between two coils of the ileum. It was very remarkable that there could not be found a single swollen solitary follicle or Peyer's patch, nor any ulcer except the perforations. The mucous membrane of the lower part of the ileum, about a foot and a half, was covered with a brownish mass of the thickness of about a line. This brownish mass appeared to the naked eye not unlike blood; after the intestine was hardened in chromic acid it was found, however, on microscopical examination, that this brownish mass consisted of a continuous layer of micrococci.

Case VII. (Case No. 16 of my series).—P. H., police constable, æt. 30. Admitted into the Fever Hospital at Islington on February 15th, 1875. Had been brought into the hospital in an unconscious state. I gather from Dr. Mahomed's notes that, according to the friends of the patient, he had been ailing about 10 days, and had not been on duty about four days previous to admission. Died the day after admission. Post-mortem examination a few hours after death. Of the chief interest was the lower part of the ileum and the beginning of the cœcum, their mucous membrane being beset with very numerous papules from the size of a pin's head to that of a hemp-seed and larger. It was the most splendid example of papular eruption in the ileum, *i.e.*, "la forme boutonneuse," that could be wished.

4. *Results of previous Observers referring to the minute Anatomy of the Intestine, Mesenteric Glands, and Spleen in Enteric Fever.*

In this chapter we wish to mention the results obtained by more recent observers with reference to the microscopical characters of the changes of the ileum, the mesenteric glands, and the spleen.

According to Rokitansky * the first stage of enteric fever consists in an acute catarrhal inflammation of the mucous membrane of the lower half of the ileum. In the second stage the hyperæmia of the mucous membrane is concentrated on the solitary and agminated glands; these swell in consequence of exudation and germination of their elements. The transverse section of a swollen patch shows a uniform degeneration of the glandular (lymphatic) tissue, and also of the connective-tissue substratum, into a medullary mass, which extends on the one hand into the mucosa propria, and on the other hand through the submucous tissue into the external muscularis. This "degeneration into a medullary mass" is the result of the multiplication and overgrowth of the glandular (lymphatic) elements into the surrounding tissues induced by the exudation. The enlarged mesenteric glands appear to be degenerated into a medullary greyish-red mass. In their connective-tissue capsule a network of varicous vessels may generally be distinguished.

In the following stage, if the degenerated mass (comprising glandular tissue and adjacent connective-tissue) does not become absorbed, it undergoes a change similar to yellow tubercular mass, being converted into a pale yellowish friable slough, which becomes gradually broken up and detached. This metamorphosis is generally accompanied by an apparent increase of the hyperæmia and swelling of the mucous membrane, especially in the parts surrounding the swollen patches. Often it is

* Lehrbuch der patholog. Anatomie, volum III, p. 215., Vienna, 1861.

The appearance in New York, 1865.

The Continent of America.—On the 10th October 1865, the "Atalanta," an English mail steamer, sailed from London, bound for New York, with a full cargo and 40 passengers, 28 cabin and 12 steerage. The next day she put into Havre, remained there one day, and received 24 additional cabin passengers and 540 steerage passengers. These persons came chiefly from Switzerland, Germany, and Eastern France. Almost all had passed through Paris on their journey to Havre, and some had stayed there several hours, others several days. At the time cholera was rapidly increasing in Paris, the month of October being the month of greatest prevalence in that city in 1865. In Havre cholera was first reported on the 18th October, and 19 deaths altogether occurred in the commune, according to the official returns. Some of the emigrants while at Havre were taken ill, and were visited and attended by Government officials. One woman died there, and Dr. Swinburne, the health officer for the port of New York, from the account of the symptoms given to him by her husband, was convinced that she had succumbed to cholera. The "Atalanta" sailed from Havre on the 12th October with a clean bill of health. On the 13th a child died from cholera on board. On the 14th, 16th, 18th, 19th, and 22nd a death from cholera occurred each day (five altogether) in one family, who, while at Havre, had stayed in the same hotel where the woman, previously referred to, had died. The ship arrived at New York on the 2nd November, when the surgeon reported 60 cases of cholera and eight deaths during the passage. The vessel was subjected to a strict quarantine, during the continuance of which 42 other cases took place and eight deaths.

Twenty days after the arrival of the "Atalanta" at New York, and eight days before this ship was released from quarantine, cholera appeared among the patients in the State Emigrant Hospital, on Ward's Island. The first person who suffered here was attacked on the 22nd of November. Other attacks followed, and from that date to the 20th December, when the disease ceased, there were 31 cases, of which 27 died. In the official report* on this outbreak no information is given as to the date of arrival of the persons attacked in New York, nor of the ships which had brought them, nor of the ports whence they had sailed. "Nearly all the cases," states Dr. George Ford, the principal physician of the hospital at the time, "occurred in the same building; nearly all were "women and children, as the building was appropriated to patients of that "class, and nearly all were labouring under acute disease or were con-"valescent from it." The appearance of cholera had been preceded by much diarrhœa and dysentery.

From the cessation of this outbreak until the 1st May 1866 no other occurrence of cholera was recorded in the city and suburbs of New York.

Ward's Island, which contains the New York State Emigrant's Refuge and Hospital, is situated 18 miles, or thereabouts, in a direct line from the quarantine anchorage in Lower Bay, where lay the "Atalanta" and the quarantine receiving and hospital ships. It appears to be quite certain that no communication could have taken place between the sick on Ward's Island and the infected crews and passengers and the sick at the quarantine station, during the 28 days that the latter were subjected to detention. Whatever the source from which the disease had originated in the Emigrant's Hospital, it could not, according to the evidence adduced, have had connexion with the "Atalanta," although the outbreak occurred not long after the arrival of that vessel.

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* *Report of the Metropolitan Board of Health, New York*, 1866. Appendix M., p. 424.

Before the outbreak on Ward's Island had come to an end, another infected ship had arrived at New York, the "Mary Ann," an American barque, which had sailed from Havre on the 25th October. She reached her destination on the 12th December, and the captain reported five deaths among the crew and passengers during the passage, four from cholera.

The appearance in New York, 1866.

No other importation of cholera into New York harbour took place until the 18th April 1866 when the steamship "Virginia," 2,936 tons, arrived in the Lower Bay, with 46 passengers sick of the disease on board. This ship had sailed from Liverpool for New York, on the 4th April. She touched at Queenstown to complete her complement, and when she left that port had on board 1,033 passengers (14 cabin and 1,019 steerage), her crew consisting of 110 men. Of the steerage passengers, 220 were German, Dutch, Danes, and Swedes, the remainder Irish, English, and Scotch. On the 12th April, the eighth day after the ship had left Liverpool, a steerage passenger, named Peter Voss, coming from Groningen, in Holland, died of cholera. This man had had several days' diarrhœa before the fatal seizure occurred and the nature of his malady was recognised. He had joined the ship at Liverpool, having travelled from his home to that port, with his family, by way of Amsterdam, Rotterdam, and Hull, leaving Groningen on the 29th March. Cholera was not known to be present in any of the places through which he passed at the time of his journey, but its appearance in Rotterdam was officially recognised on the 8th April, about a week, or probably even a less time, after he had been in that city. From the 12th to the 18th April, the date of the ship's arrival at New York, 33 of the passengers and two of the crew had died of cholera, and, as already stated, 46 passengers were ill of the disease when she reached her destination. During the detention of the passengers 46 days in quarantine, 144 other cases occurred among them, making altogether 190 cases received into the hospital ship. Of these cases 72 died, the whole number of deaths, from the commencement of the vessel's voyage from Liverpool to the termination of the quarantine at New York, being 110.*

Two days after the "Virginia" had reached New York the steamship "England" arrived in the harbour. She had no cases of cholera on board at the time, nor did any cases occur among the crew and passengers during 20 days' detention in quarantine. But many cases had occurred at sea, rendering it necessary for the ship to put into Halifax, Nova Scotia, and there the disease was communicated from the ship to the shore in several instances of remarkable interest.

The steamship "England," 3,440 tons burthen, bound for New York, sailed from Liverpool on the 28th March 1866. She carried from the Mersey 16 cabin, and 791 steerage passengers, and had a crew of 122 officers and men. Touching at Queenstown on the evening of the 29th, she received on board there, in addition, 1 cabin, and 393 steerage passengers, and put to sea again as soon as the embarkation was effected. The total number of persons at that time on board the ship was 1,322. Of the passengers who joined the "England" at Liverpool 465 were emigrants from the Continent of whom the precise

* *Report of the Commissioners of Quarantine Health and the Officer of the port of New York* (Dr. John Swinburne) for 1866. I have adopted the figures given in Table B. of this Report (p. 71). There are certain discrepancies between this Table and the text of this Report. I have adopted also the statement made in this Report respecting the number of foreigners among the passengers on board the "Virginia," namely, 220, in place of the number (465) given in a previous Report of mine, to which reference is made (p. 64).

the medullary intumescence, following the catarrhal enlargement, it is impossible for the unaided eye to distinguish between cortex and medulla. The microscopical examination shows that the follicular (adenoid) tissue is the chief seat of change, "the lymphatic sinuses, and "especially the connective-tissue, presenting only a moderate infiltration "with Typhuszellen."

In the lymphatic cylinders of the medullary part an enormous distension of capillary blood-vessels is met with (*see* Hoffmann). Rindfleisch maintains that this seems to be generally characteristic of the "medullary condition."

Besides this, a conspicuous "plugging" ("Verstopfung") of many capillary loops, as well as of the larger vascular branchlets, frequently occurs with a dark granular mass, the nature of which Rindfleisch was unable to determine.

"Very striking," says Rindfleisch, l. c., p. 323, "is the condition of "the adenoid trabeculæ, all of them being three and four times as "thick as in the normal condition, the nucleated parts especially "being swollen, and the nuclei vesicular." . . . . . "In many "places the continuity of the reticulum is interrupted, and in its place "lie roundish masses of cells. The mode of cell-formation is principally "that of simple division. Besides this, however, often endogenous cell-"formation occurs." Rindfleisch here, of course, refers to the large cells containing numerous nuclei, which have been noticed also by previous authors (*see* Hoffmann).

5. *Early Changes in the Lymphatic Follicles of the Ileum.*

I will commence my own observations with describing the changes the lymphatic follicles—the solitary ones, as well as those of the Peyer's glands—undergo in the early stages of enteric fever.

Besides the distension of the blood-vessels of the parts surrounding the lymphatic follicles, and of those in the mucosa of the adjacent parts, the earliest changes that have come under my observation, are those which consist in simple swelling of the solitary glands, "la forme boutonneuse" of French authors, as in case VII. By carefully examining several sections I can trace the development of these "swollen solitary glands." I see in some places small accumulations of ordinary nucleated lymph-corpuscles, *i.e.*, cells composed of a more or less spherical nucleus, which stains deeply in hæmatoxylin, and is surrounded by a thinner or thicker crust of granular protoplasm. This appearance is found in the tissue of the mucosa propria between the Lieberkühn's glands; that is to say, at some places the lymph-corpuscles of the normal tissue of the mucosa have increased in a conspicuous manner. The greater the number of these lymph-corpuscles the more the Lieberkühn's glands give way, or, properly speaking, become compressed, their epithelium at the same time becoming detached and broken up into small groups of cells; and finally, as the number of lymphoid cells becomes still greater, the epithelial cells of the Lieberkühn's glands become hardly discernible as such. Only nests of cells indicate the place of the former tubular glands. At these points the mucosa is thicker, and therefore its surface is elevated above the surrounding part.

From these places I can trace others, where the number of lymph-corpuscles has increased to such an extent that the mucosa forms a distinct prominence; the Lieberkühn's crypts are hardly discernible; the villi on it are so shortened and their base is so broad, that it is quite evident that a great deal of traction has been exerted on them; this becomes clear, if it is borne in mind that as the number of lymph-corpuscles increases in

a given area, the mucosa increases in depth, *i.e.*, in its vertical diameter, and in doing this it necessarily encroaches on the corresponding villi.

The next step in the process is the production of those large spherical accumulations of lymphoid corpuscles which project through the muscularis muscosæ into the submucous tissue, where they are limited by a lymph sinus. These produce those more considerable prominences of the mucosa which correspond to the swollen solitary glands of the size of a hemp seed and larger.

In stating that this is the "next step," it must be borne in mind that there are intermediate stages, of which the last-mentioned form is the terminal one. As regards the relation between these stages and the solitary and agminated follicles, I differ from other observers.

I do not mean to deny that the solitary glands become swollen, but I do deny that the papular prominences of different sizes of a pin's head to that of a hemp-seed and larger, as seen in early cases, are all swollen follicles. I have two reasons for saying so: first, and this is the stronger reason, I can trace the development of these prominences back to simple small accumulations of lymph corpuscles in the mucosa; I can see how ordinary mucosa—*i.e.*, provided with Lieberkühn's glands, and covered with villi—becomes gradually, in a given area, more and more infiltrated with lymphoid cells, and how the ordinary aspect of the mucosa gradually changes into that of a tissue which seems to be entirely, or in great part, composed of lymphoid cells. The second reason is this: I am not aware that in man so many solitary follicles normally exist in the ileum. They are extremely scarce in the ileum of animals, and in man I cannot find them by any means in such numbers as one would expect if all those prominences were due to solitary glands. I am therefore of opinion that during the stage of catarrhal inflammation the mucosa becomes, in certain more or less well defined areas, infiltrated with lymph-corpuscles to such an extent, that it appears to contain tumours. It would be unjustifiable to enter into a discussion whether these lymph-corpuscles owe their origin to emigrated colourless blood-corpuscles, or whether they are offsprings of the lymphoid corpuscles which are contained normally in greater or smaller numbers in the mucosa, both being morphologically indistinguishable. In the same way as portions of the mucosa become transformed into tumours of lymphatic tissue, the pre-existing solitary lymphatic follicles also increase in size; they seem to be composed of ordinary lymph-corpuscles; the number of which seems to have increased principally in the central parts, for the peripheral zone and the tissue surrounding the follicle is seen to be more distinctly composed of concentric layers of adenoid tissue (*i.e.*, fibrous meshwork containing lymph-corpuscles) than it is under normal conditions.

The change which immediately follows the simple increase of lymphoid corpuscles consists in the presence of a great number of cells having nuclei, considerably larger and more transparent than those of ordinary lymph-corpuscles; they look in this condition more like nuclei of endothelial cells than of lymph-corpuscles; the cell-substance surrounding this enlarged nucleus is an opaque protoplasm. It sometimes appears at first sight as if there were present two kinds of cells; viz., (1) small cells with very little granular protoplasm surrounding the nucleus, which is more or less of a spherical shape, and stains deeply in hæmatoxylin; and (2) cells, two, three, and four times as large, composed of a rather opaque, coarsely granular substance, and containing an oval transparent large nucleus, which does not stain in hæmatoxylin, and is invariably situated peripherally; occasionally, but rarely it is divided into two. On closer examination, however, all intermediate forms

between the two are found, so that there is no doubt about the second kind of cells being derived from the first kind. I refer the reader to Fig. XLI. which is taken from a Peyer's patch.

In some places the enlarged cells contain in addition to the above-mentioned large ovoid nucleus, one or even two smaller spherical nuclei, which stain deeply in hæmatoxylin, and which are perfectly identical with the nucleus of an ordinary lymph-corpuscle. Occasionally the spherical nucleus is not simply surrounded by the opaque cell substance, but lies in a clear vacuole. Comparing these elements with one another, one cannot help coming to the conclusion that the enlarged cells have taken up the small lymph-cells, and of the latter only the nucleus has retained its existence as such within the cell it has been taken up by.

In this stage the trabeculæ of the matrix of the adenoid tissue are not thickened or enlarged, as represented by Hoffmann, Rindfleisch, and others, but on the contrary the tissue is rarefied,—at least, where one has an opportunity of seeing the so-called adenoid reticulum, it always appears to be rarefied, *i.e.*, its meshes are very much larger than in the normal condition. It may also be stated in this place that, according to my recent observations of the lymphatic follicles of the intestine, as well as of the mesenteric glands, the so-called adenoid reticulum in the normal condition *is not a network of fibres, but a honeycomb of membranes*, which, when seen in the bird's-eye view, appear to be transparent, more or less hyaline, or occasionally very slightly fibrillar (see Fig. XLI.). I agree with Bizozzero, that in the adult, as a rule, the stroma does not contain such large numbers of nuclei as is generally represented. What I find is, that there are endothelial-looking cells closely applied to the stroma, the nuclei of which cells are larger, more transparent and ovoid when seen in profile than the ordinary spherical nuclei of lymph-corpuscles ; the latter stain more deeply in hæmatoxylin than the former. It must be added, however, that there are intermediate forms between the ordinary lymph-corpuscles, and the endothelial-looking cells containing a large nucleus. In consequence of this it would therefore appear as if in the abnormal condition the endothelial-looking cells had increased in number, and become conspicuous by their substance being very distinct, and somewhat opaque. There is, as far as I can see, nothing against the assumption, that many of the ordinary lymph-corpuscles have become transformed into the large cells. The number of the enlarged cells constantly increases, until the adenoid tissue seems to contain almost no other lymph-corpuscles than the large cells with transparent ovoid nuclei. I have seen this appearance in many parts of the swollen Peyer's glands.

The cells continue to enlarge, so as to represent opaque elements, each containing a large ovoid transparent nucleus, situated peripherally, besides a variable number of spherical nuclei, either isolated or in groups, simply embedded in the substance of the large cell, or enclosed in a vacuole. In the latter case, the nuclei may be occasionally seen to be surrounded by protoplasmic substance of their own, thus resembling small lymph-corpuscles. Besides this, there are found, within the larger elements, larger or smaller lumps of a substance similar to that of the spherical nuclei. It seems reasonable to maintain that some of the spherical nuclei become broken up within the large elements.

Not only in the Peyer's glands, but also in the mucosa itself, the lymphoid corpuscles undergo those changes. In Figs. XLII. and XLIII. I have represented very accurately these different kinds of elements, and I therefore refer the reader to the explanation of these figures.

The most natural interpretation of the various forms under which these cells appear is, I think, the following : The enlarged lymph-cells incorporate the smaller ones, and this helps to increase their size ; of

the nuclei of the incorporated cells, some become broken up, others retain their existence and represent the nuclei of ordinary lymph-cells which make their appearance in that enlarged cell; this latter having become vacuolated, gradually transforms into a vesicle, which at one point of its periphery still possesses the original ovoid transparent nucleus. The last form we shall meet with abundantly in a somewhat later stage.

Thus we appear to have a kind of endogenous formation of lymphoid cells, somewhat different from the ordinary mode of endogenous cell formation, according to which the nuclei of the daughter-cells are the offsprings of the nucleus of the mother-cell. In the present instance I am inclined to oppose such a view, as the very characteristic ovoid transparent nucleus of the large lymph-corpuscles of the early stage undergoes hardly any alteration during the succeeding stages. Of course, the lymph-corpuscles do not all run through all the stages enumerated; many of them after having become enlarged gradually break down into a granular mass. This I have seen to happen in places where the adenoid tissue had so much altered that it seemed to be composed entirely of very large cells more or less closely aggregated; of blood-vessels, or even of a stroma, there was no trace.

Large portions of the tissue of Peyer's glands and of the mucosa frequently present this aspect, as *e.g.* in Case I., in which in many places the fibrous stroma had altogether disappeared.

Some blood-vessels of the submucosa contain large cells similar to those described above.

Before continuing our description of the further changes of the lymphatic follicles, we must mention here a peculiar change in them not noticed by previous observers. This refers to the central portion of the enlarged follicles (both solitary and agminated, in these last every one of the follicles being often affected,) becoming so altered, that instead of a dense accumulation of lymph-corpuscles, we find a tissue of a more or less spongy appearance, consisting of anastomosing broad trabeculæ, between which are contained smaller or larger areas of a transparent substance. I must here refer the reader to Fig. XLIV. in which I have tried to represent these appearances as accurately as possible. The periphery of the follicle consists, as is seen in the drawing, of the ordinary adenoid tissue; towards the centre the substance of the follicle consists of (*a*) trabeculæ, which in some parts include a capillary blood-vessel, while in others they are represented by a more or less opaque granular substance in which are embedded smaller or larger nuclei; and (*b*) transparent parts occupied by very transparent nucleated cell-plates, which, towards the periphery, become identified with the larger nucleated lymph-corpuscles represented in the drawing. With regard to these cell-plates, it is evident in many places that they have a curved shape, so as to line their respective lacunæ. Still nearer to the centre the cell-plates are seen to become greatly enlarged, their substance at the same time changing into a less transparent, distinctly granular substance, containing, instead of one large nucleus, several small nuclei. In still further advanced stages of the process the centre of the follicle is in so far different that it contains within the meshes of a framework, composed of more or less elongated nucleated cells or bands, *including capillary blood-vessels*, only multinuclear (10 to 30 nuclei and more) protoplasmic masses, *i.e.*, true "giant-cells."* These giant-cells may be traced

* These are different from the large cells previously mentioned, containing several nuclei. We shall have occasion to mention several times hereafter large lymph-corpuscles, in which there are several, even many, nuclei and nucleated cells, but these are perfectly different from "true giant-cells."

towards the periphery, to the cells containing one large nucleus. The giant-cells are seen to be of different sizes (see Fig. XLV.), and many of them have a distinct tubular shape; this can easily be made out in sections by noticing the arrangement of the nuclei which are chiefly disposed along the periphery of the cell.

In hardened preparations the central spongy part of the follicles first named possesses a very diminished cohesion; it is very liable to break down, so that the bands above referred to as composed of nucleated cells and containing the capillary blood-vessels are almost the only residues of it. These changes were observed in follicles both of solitary and Peyer's glands of the ileum in Case No. I., which terminated on the seventh day, and, as the reader remembers, was of an unusually rapid progress, the ileum already containing an ulcer.

Preparations, like the one I have exactly represented in Fig. XLV. doubtless remind one of "the reticular giant-cell-tubercle," and the question is suggested whether Case I. was really one of enteric fever, or whether it was not rather one of acute miliary tuberculosis. Examining the case more carefully, however, the assumption that the histological appearances are those of "giant-cell-tubercle" must be dismissed, for apart from the fact that the stroma of the latter is altogether different from that of the giant-cell-follicles, described above, there is this additional evidence against it, that in the present case the structure in question is provided with blood-vessels. Thus the only feature that is left common to both —to "the giant-cell-tubercle and "the giant-cell-follicle"—are the giant-cells. In the present position of the question of the origin of giant-cells I scarcely think any observer will regard their presence as evidence of the "tuberculous" nature of the above-named follicles; besides which, in the very same specimens of the ileum which contained follicles changed in the manner represented in Fig. XLV., I have seen isolated true giant-cells in the mucosa propria. In this latter, as well as in the submucous tissue, there were several examples of giant-cells in connexion with peculiar cylindrical bright bodies (I have met them five times altogether in my sections), which are probably of a vegetable nature; they are composed of a central transparent part and a peripheal highly refractive thick crust. I must refer the reader to Figs. XLVI$_{i.}$ and $_{ii.}$ The giant-cell is seen to adhere very closely to this foreign body, and seems almost to surround it. Both the giant-cell and the foreign body appear to be contained within a definite space which contains other cellular elements besides and is bordered by a fibrous wall. There are always one or more capillary blood-vessels around it. That the foreign body is only an accidental feature, will I think be conceded; and likewise that the giant-cell surrounding it owes its origin to the irritation set up by the body in question. That an irritation of this kind should change an ordinary lymph-cell into a giant-cell seems to be explained by assuming that in this particular case there existed, from some unknown cause, a great predisposition of lymphoid cells to become converted into true giant-cells.

The microscopical evidence does not, however, rest here, for there are certain changes of the ultimate branches of arterial vessels, which I found in the ileum of Case I. as well as in the enlarged spleen of two undoubtedly enteric cases (Case II. and III.).

They are as follows: In almost all the follicles of the ileum (Case I.) that showed the transformation of their centres into the spongy-looking substance described above, one or more blood-vessels, apparently ultimate branches of arteries or arterial capillaries were met with in or near the centre of the follicle, in which there was present between the more or less distinct lining endothelium and an adventitial thin nucleated mem-

brane (endothelial membrane), a yellowish, transparent, and homogeneous substance of greater or less thickness and of a variable extent. Generally this colloid-looking substance stains very slightly with logwood, and is arranged apparently in more or less disconnected lumps of different sizes and of an oblong or spherical or irregular shape (compare Figs. XLVII. and XLVIII.). This material produces a considerable thickening of the wall of the vessel, the lumen of which becomes more or less distorted, and greatly compressed; in many cases it comes to be situated excentrically, from the presence of this material in greater quantity at one side of the vessel than at the other. It is probably possessed of less resistance than a lymph-corpuscle is able to overcome, for lymphoid (migrating) elements may be seen occasionally embedded in it. That these changes of the blood-vessels are of material importance to the tissue these vessels supply, *i.e.*, the lymphatic follicles, and perhaps even represent one of the direct causes of the changes which take place in them will hardly be denied, considering the frequency of their occurrence, and considering that the permeability of those vessels may thereby become greatly diminished or may even altogether cease.

In this case (Case I.), as well as in others (II. III. and IV.), the submucous tissue of the ileum, particularly of those parts which are in the neighbourhood of swollen lymphatic follicles, presents very distinct signs of a more or less intense œdema, viz., the blood-vessels are distended and filled with blood, the lymphatic vessels, and especially the interfascicular lymph-spaces, are also widely distended, and contain large coarsely granular lymph-corpuscles with one large, or two or three small, nuclei, and a finely granular substance—coagulated plasma. Among the cells just mentioned are many which show distinct vacuolation; in some this is so far advanced that the cells present the appearance of a signet-ring, the nucleus being included in the thicker part of the periphery.

The connective-tissue corpuscles lining the interfascicular lymph-spaces may be recognised as granular, rather swollen cells, their nucleus occasionally constricted.

I was very much struck in these specimens with the distinct œdema of the Meissner's and Auerbach's ganglia. In general it is surprising for how long a period the ganglion cells of the Meissner's plexus retain their normal aspect; for even in parts in which the tissue has become crowded with lymph-corpuscles, and in which disintegrative changes have already advanced to a considerable extent, groups of ganglion cells may be seen of almost normal appearance, although all the elements around them have considerably changed their aspect.

6. *Organisms found in the Intestinal Mucous Membrane in the Early Stages of Enteric Fever.*

Before proceeding further I will put together all the facts I have been able to ascertain with regard to the presence of minute organisms in the tissue of the mucous membrane of the ileum in the earlier stages of the disease, *i.e.*, before the time of the general ulceration. I am prepared to hear some readers express surprise at the relative want of connexion in the results to be narrated presently, as well as at my being inclined to draw definite conclusions with regard to the identity of the contagium of enteric fever with a low vegetable organism; but I hope to be able to show that organisms occur in the mucous membrane of the intestine in enteric fever in such numbers and so definitely arranged that their importance cannot be questioned for a moment.

I commence with the earliest case I have examined, *i.e.*, Case I., in which death ensued after six days. I think it unnecessary to give

a long and exhaustive description of all the minute details, for a reference to the plates, in which I have endeavoured to reproduce the corresponding appearances as accurately as possible, will enable the reader to understand all that relates to the subject. In the mucosa of these parts of the ileum, which to the unaided eye do not present any conspicuous changes, except slight increase of thickness in consequence chiefly of greater succulence, the Lieberkühn's crypts contain in their lumen corpuscles like those represented in Figs. II., III. and XI; they are highly refractive, and of a greenish-yellow colour; they are of different sizes, from that of about twice the size of a human coloured blood corpuscle down to that of a very minute granule (*see* Fig. XI.); they are mostly spherical, or hour-glass or kidney-shaped, and seem to be held together by a transparent connecting substance. At the margins of lumps composed of these bodies, besides the hour-glass and kidney forms, dumb-bells are also seen, and these, according to all our experience, show that the corpuscles in question multiply by transverse division. They are generally contained in the lumen of the Lieberkühn's crypts in smaller or larger masses, and in preparations stained with hæmatoxylin appear of a rather deep olive-green colour. In most of the Lieberkühn's crypts I find them situated either at or near the bottom of the gland, but I have sometimes seen them at the entrance *i.e.*, at the mouth of the crypt. From what has been already stated it is evident that these bodies are of the nature of organisms; they are found of various forms; I refer to Figs. IV., V., VI., IX. and XII. The drawings show that the corpuscles in question are enveloped in structures of a more or less tubular shape, the wall of which is a distinct membrane, showing either irregular constrictions or thickenings (the result of shrinking probably caused by the action of the hardening reagent). Taking into consideration appearances like those represented in Figs. VII., VIII. and X., one cannot help coming to the conclusion, first, that we have here to do with a fungus which possesses mycelium-threads of very unequal joints (Fig. VIII.); secondly, that in some parts of these threads, probably the terminal parts, their contents split into macrogonidia, as in Figs. IV., V., VI., IX. and XII.; or microgonidia, as in Fig. X.;—further, that the gonidia become discharged, the thread having become broken, as in Fig. VII.; and finally, that the gonidia when discharged undergo rapid division, so as to form a kind of zoogloœa, that is to say, groups of small spherical organisms held together by an interstitial gelatinous substance. It is remarkable that the appearances presented by this organism correspond closely with those described by Cohn as characteristic of the vegetation discovered by him in well-water in a district of Breslau famous for enteric fever—I mean Crenothrix polyspora.*

* In 1870, Professor Cohn described a very peculiar microphyte, *Crenothrix polyspora*, which he found in well-water in a certain district in Breslau famous for the frequent occurrence of enteric fever amongst its inhabitants. The water in question was found to contain numerous yellowish-brown flakes, which on careful examination were seen to consist of interweaving threads, of different length, and having a straight or winding course; they contain in their interior numerous cells, which are externally covered by a kind of sheath—probably an excretion of the cells,—through which they often project. The top cells are always considerably longer than the others, the next lower frequently possess lateral branch-like dilatations. The cells contain a colourless finely granular protoplasm. The threads are of various thickness; some of them terminating in a club-shaped swelling. Reproduction takes place thus: the plasma of the individual cells divides by several horizontal and vertical fissures; the products either remain large, and represent macrogonidia, or they continue to divide, thus forming very small microgonidia. The cell partitions then become absorbed, so that the gonidia come in contact with each

That all these peculiar corpuscles—from the large ones represented in Figs. II., III., IV. and VII., to the small micrococci seen in Figs. VII., X. and XI.—are one and the same kind of organisms, is evident not only from their general aspect, but also from the numerous intermediate forms as well as from the natural history of Crenothrix polyspora. The development of these organisms and their production of macro-and micro-gonidia, and the consequent formation of zoogloea of micrococci, has been investigated most satisfactorily by Professor Cohn. I cannot therefore admit that a definite line exists between a mycelium fungus and micrococcus in the form of zoogloea, for, as we saw just now, the latter originates by the division and multiplication of the spores produced by the former. In our case we find, indeed, at the mouth of some Lieberkühn's crypts, as well as on the free surface of the intestinal mucous membrane, masses of micrococci according to all appearances analogous to those in Fig. X., and therefore most probably offsprings of the gonidia just mentioned.

The products of the fungus under consideration are found, however, in other parts of the mucous membrane, as well as in the Lieberkühn's crypts; I have seen the gonidia-form and the micrococci in larger or smaller masses in the tissue of the mucous membrane in close proximity to Peyer's glands. The micrococci especially occur in large masses in the lymph-spaces surrounding the Lieberkühn's crypts, and in the tissue next to it, as represented in Fig II.

It does not, however, rest here, for I have found the same organisms, though rarely, in lymphatics, but especially in veins and venous capillaries, not only of parts next to Peyer's and to the solitary glands, but also in the mucosa and submucosa of the surrounding portions.

In Figs XIV. to XIX., I have represented blood-vessels containing corpuscles in every respect identical with the spores contained in the Lieberkühn's crypts. That the corpuscles in question are either blood-corpuscles or their derivates (hæmoglobin-particles which have become confluent to larger bodies, or which have become broken up into small granules) cannot be supposed for a moment, considering, first, the identity between the bodies represented *e.g.*, in Fig. XVII., with those in Fig. IV.; secondly, the improbability of blood remaining unchanged in the vessels (Fig. XIX.) after the specimens have been treated with chromic acid, spirit, &c.; and thirdly, that particles similar to the small particles of Fig. XV., are contained in colourless blood corpuscles, and are identical with particles, to be described hereafter, which resist acids as well as caustic potash. From what has been already said I think I am justified in maintaining that the spores and micrococci find their way from the surface through the Lieberkühn's crypts into the lymphatics and blood-vessels. The fact that these are found in relatively so late a stage of the

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other; these crowd together at the extremity of the thread, which (extremity) in the meantime often becomes swollen, and are finally discharged. After this, the next lower cells commence the process of the formation of gonidia. The individual gonidia are colourless, oval or spherical, and show occasionally a transverse constriction—significant of division; they do not possess a distinct membrane, and they exhibit a slow rolling movement. Often they remain, for some time, lying at the mouth or broken end of their respective threads, similar to a palmella-mass. The macrogonidia appear to originate from the broad, the microgonidia from the thin threads. It is probable that the gonidia reproduce the Crenothrix threads. A remarkable fact, observed by Cohn, is this—that the microgonidia, which are very often met with in forms indicating division into two, (dumb bells,) and which in their general appearance completely resemble spherical micrococci, form zoogloea masses, which, just like those of micrococi, consist of small spheres held together by, and imbedded in, a gelatinous interstitial substance. In my observations on the microphyte occurring in sheep-pox, I have stated a similar fact, viz., that spherical micrococci are produced by division of conidia originating from a hyphomycetes-fungus.

disease as after six days, does not prejudice the supposition that the same thing may have taken place in the earlier stages of the disease, for why should not the absorption of these elements, if present, continue for some time especially in parts which are not yet altered very much? On the contrary, to my mind, it appears most probable that the same has been going on also in those parts which are now changed, swollen, and infiltrated, before they were so changed.

I come now to mention the presence of masses of micrococci in the different parts of the intestinal mucous membrane of other cases. In Case I., as we have seen, they were found on the surface of the mucous membrane, in the mouth of the Lieberkühn's crypts, and also in lymph-spaces around them; they were also very numerous in Case II., in which death occurred the 11th day; and somewhat less so in cases III. and IV. In case II. I found them as zooglœa-masses, not only around the swollen lymphatic follicles, but also in portions of the mucous membrane, at a little distance from them, which appeared almost normal to the naked-eye inspection.

The micrococci, found in large masses on the free surface, may be traced through the epithelium between this and the stroma of the villi, or that of the summits of lymphatic follicles, *i.e.*, those parts of lymphatic follicles which project into the proper mucosa, and extend to the free surface. In Fig. XX., masses of micrococci are seen on the free surface of a villus; they penetrate through the epithelium, and accumulate in a space between the epithelium and the stroma of the villus. In Fig. XXV. they are seen to penetrate from the free surface into the mouth of a Lieberkühn's crypt, and also through the epithelium into a space between it and the matrix of the subjacent summit of a lymphatic follicle. These spaces which occurr underneath the epithelium of the surface, owe their origin to the epithelium having become loosened over greater or smaller areas. This fact, which has been noticed by previous authors, is evidently due to the condition of hyperæmia and œdema of the mucosa, and the consequent accumulation of fluid at that point where there is least resistance. This abnormal condition of the mucous membrane, though slight, is found in many parts of the mucosa —even at a distance from Peyer's glands—during a very long period of the disease, a period extending far into the stage of ulceration.

Further, I find the same masses of micrococci in all depths of the lumen of the Lieberkühn's crypts, whence they penetrate through the lining epithelium into the surrounding lymph-space, which appears more or less distended; spaces at or near the bottom of the crypts are favourite places for the accumulation of these masses, see Figs. XXI.—XXIV. From the lymph-spaces around the bottom of the Lieberkühn's crypts, I have been able to trace them into lymphatic spaces of the adjacent parts of the mucosa, especially if these parts are composed of adenoid tissue, see Fig. XXX.

They are also found in the walls of veins, whence they actually penetrate into the lumen of the vessel. Fig. XXVI. shows groups of micrococci in the wall of a vein; Figs. XXVII. and XXVIII., show the same inside a vessel.

In all these places the larger and thicker the masses of micrococci are, the more decided is their brownish-yellow colour; the thin masses are very pale. Another noteworthy feature is that they form spherical lumps, exactly like those described in the second chapter as observed in the alvine discharges.

It is clear, from the foregoing, that we have to do with an absorption of masses of micrococci from the surface into the lymphatics and blood-vessels. It might be urged that the presence of the micrococci in the

tissue is due to post-mortem changes; but this objection must be abandoned, as it is impossible to imagine that micrococci will penetrate passively from the surface of the intestinal mucosa into the depth of the tissue in a definite manner, as we have seen to be the case, besides which the tissue itself appears to be perfectly well preserved, *i. e.*, the outlines of the elements are sharp, and their general aspect very far from that of a state of decomposition. Another very important point with regard to the presence of the micrococci during life is their existence in the fresh alvine discharges, as described in the second chapter; and finally, we may adduce Case VII., where the mucous membrane of the lower part of the ileum, which has been placed in chromic acid about one hour after death, was covered with a thick and very closely-adherent crust of the same micrococcus. When examined under the microscope, it was found that in this case the masses of micrococci extended into the Lieberkühn's crypts, and partly also into the tissue of the mucosa; the epithelium of the villi was in many places more or less raised from the subjacent tissue, and micrococci were found in the space between in a manner similar to that described above. I think all these facts furnish sufficient evidence against the supposition that the presence of the masses of micrococci is due to post-mortem changes.

7. *Changes of the Lymphatic Follicles in Later Stages (Ulceration).*

In the last chapter but one we mentioned the disintegration of enlarged lymphoid corpuscles of the lymphatic follicles and of the mucosa. Shortly before and during this stage, in which the elements of the tumor break down, so as to be either absorbed, or, in more serious cases, to be gradually detached as a slough, thus leaving an ulcer, there is also another important change; this consists in the reticulum of the lymphoid tissue becoming, in some places, transformed into a very dense feltwork, of stiff, highly refractive fibres, between which the original cellular elements gradually disappear, by first losing their distinct outlines, and then becoming disintegrated. In Fig. LV., I have represented this change; the preparation was made from the mesenteric gland, where this change is exactly the same as in the intestine. Thus, one finds in many swollen Peyer's glands, at the beginning of the necrotic condition,—which, as we shall presently see, is easily recognized under the microscope,—larger and smaller portions showing the change of the reticulum just mentioned.

The question now presents itself how are the necrotic—retrogade—changes, induced and on what do they depend? Almost all observers, including Hoffmann, assume that the retrogade changes are due to the failure of the circulation in the lymphatic follicles. The cellular elements of the follicles having increased in size and number to an enormous extent, produce a compression of the blood-vessels, which causes in its turn a gradual waste of its structural elements; for this reason one can hardly see the blood-vessels in the swollen follicles. The compression of the blood-vessels necessitates a decrease in the supply of nourishment, and a disintegration of the elements of the gland. Now in many parts of the follicles the blood-vessels have become much narrower, or even seem to have disappeared; and it stands therefore to reason that the tissue which was supplied by those vessels will suffer considerably, and will even die. But I must decidedly oppose the statement that the ulceration in the intestine in enteric fever is due solely to compression of blood-vessels. There are several very strong reasons against such a theory. If the ulceration were due merely to compression of the blood-vessels, how does it happen that the typhoid

ulcer,—" Typhusgeschwür "—is of such a characteristic appearance, not met with in any other kind of ulceration of the intestine,—*e.g.*, in follicular ulceration subsequent to catarrhal inflammation, or in tuberculous ulcers—although all cases are alike preceded by swelling? Further, actual observation proves that retrograde changes occur in places in which the blood-vessels are, on the contrary, distended, as is the case in the beginning of ulceration in places somewhat distant from swollen follicles. From Case V. I obtained specimens of all the different stages of the disease (see Chapter 3): from the swelling of the lymphatic follicles, to the time of their complete destruction and disintegration so as to leave behind a more or less deep ulcer; and in these I have frequently met with appearances which seem to prove conclusively that in many places the compression-theory cannot be upheld. These appearances are as follows:

(*a.*) One meets with swollen Peyer's glands, in which only the very deepest parts show just the first signs of retrograde change, the reticulum being much closer, the outlines of the enlarged lymph-cells somewhat indistinct, and the cell-substance pale and fading; the blood-vessels all through the glands are distinct; underneath the glands is ordinary fibrillar connective-tissue arranged in bundles, forming the deep part of the submucous tissue. In a preparation that I have before me, while I write, I find just at the boundary, as it were, between the Peyer's gland and the deep submucous tissue, a large blood-vessel (vein) completely blocked up by a dark-brown amorphous material including fibres and a few lymphoid corpuscles or masses of coloured blood corpuscles. A similar dark-coloured material occupies the distended interfascicular lymph-spaces of the connective-tissue of the submucosa, and is present also in one or the other lymphatic. The tissue next the parts containing this dark-coloured material is in a necrotic condition, *i.e.*, the outlines of its elements are fading away, or the elements themselves giving place to a granular mass. This last change extends also on the adjacent lymphatic tissue and the bundles of ordinary connective-tissue. (*b.*) It often happens that within the swollen Peyer's gland, especially in the more superficial parts, a small arterial branch may be met with, the lumen of which is occupied by the same dark-coloured material, which, however, presents here a more uniform appearance. Probably from having been, like an embolus, subjected to a certain amount of pressure from the blood-column behind, it does not appear to be composed of particles of different sizes, but is more a uniform block of homogeneous substance. In the neighbourhood of such a vessel the tissue is seen to contain more or less of the same material. (*c.*) In parts in which the retrograde changes have already commenced, as well as where they have not yet begun, a distended blood-vessel—generally a distended vein, but I believe I have occasionally recognized a very dilated arterial vessel—may be seen, the lumen of which though perfectly permeable contains in its wall, at one or more points, an infiltration of the dark-coloured material already mentioned. The interesting fact about this is, that if this material is traced for some distance into the surrounding parts, these exhibit the morphological characters of retrograde change enumerated above; but beyond this distance the elements appear to be unaltered, *i.e.*, the aspect of the enlarged lymph-corpuscles and of the stroma is still the same as in the earlier stages; thus showing that the retrograde change bears a definite relation to this same material. Finally, (*d*) there are places where comparatively few portions of the Peyer's glands or of the solitary lymph-follicles show retrograde changes of their substance, whereas in the parts surrounding the lymphatic gland there is a deposition of dark material in the interfascicular lymph-spaces,

and a consequent breaking down of the corresponding parts; and this change gradually extends to the neighbouring lymphatic follicles. I refer the reader to Figs. XXXV., XXXVIII., XXXIX., XL., and LIII. and their explanation. Fig. LIII. is from the mesenteric gland; but precisely the same appearance is met with quite as frequently in the intestine. I may mention that the mesenteric glands afford additional evidence that the retrograde changes are not due to compression of blood-vessels, as these are decidedly dilated.

From this it is evident that I do not regard the retrograde changes of the intestinal mucous membrane due to compression of blood-vessels, but to the deposition, probably by exudation from the vessels, of a peculiar dark-coloured material, in connexion with, and around which the tissue undergoes necrotic changes. It is obvious that if an exudation takes place, the exuded material will be found accumulated chiefly in the lymphatic spaces of the tissue. The important question now arises, what is the nature of the dark-coloured material, so often mentioned? As I said before, it is of a more or less brownish-yellow colour; it stains very deeply, almost black, with hæmatoxylin, and presents the appearance of a heap of amorphous particles of different sizes intermixed with a more regularly granular material—micrococci, and contains in some places coagulated fibrin. I have seen specimens where the deep stratum of the submucous tissue contained a very abundant network of lymphatic spaces filled chiefly with coagulated fibrin; the tissue around which was more or less disintegrated. In some places it is possible to recognise groups of larger spheroids (*see* Fig. XXXV.).

If the sections containing the dark-coloured matter are subjected to a thin solution of caustic potash (from 2 to 30 per cent., it is seen that both the small granules and the groups of larger spheres remain unaltered, as they also do when treated with acids, ether, chloroform, absolute alcohol, oil of cloves, &c., thus clearly showing that they are not belonging directly or indirectly to the tissue of the intestine, but that they are of foreign origin. I do not know any other bodies except minute organisms that can be thought of in connexion with them. Besides being found free, they are also seen enclosed in cells, within blood-vessels and in lymphatics, and in the tissue surrounding them. They are found most abundantly where the necrotic changes are most advanced. The large spheres are of a bright appearance, and show signs of division, being hour-glass shaped and forming dumb-bells, and are thus split up into smaller spheres; from these to the minute micrococci all intermediate forms may be observed. Groups of the larger spheres, after being acted upon by caustic potash, exhibit a striking resemblance to the larger micrococci described in a former chapter as occurring in the alvine discharges of enteric patients. With regard to the morphological characters of these organisms, I refer the reader to Figs. XXXI. to XXXIV., and XXXVI.

A very striking instance of the presence of masses of micrococci in the blood-vessels of parts of the mucous membrane undergoing necrotic changes is shown in Fig. XXXVII., which represents blood-vessels blocked up by micrococci; the micrococci also extended into the surrounding parts for some distance.

We have hitherto been considering the causes and the nature of the necrotic changes in general, it remains now to add that these changes occur simultaneously at different points of the same gland, and by spreading on all sides give rise to the disintegration of large masses of the tissue of the lymphatic glands and of the mucosa. The necrosis does not, however, spread only from the depth towards the surface, but may begin independently in the superficial parts of the mucosa, and spread towards the depth so as to meet that commencing in the latter.

I have seen this take place on the surface of Peyer's and of the solitary glands, (the necrosis being still limited to the deepest parts), which had become deprived of the epithelium covering the summits of the follicles, while masses of micrococci were seen to penetrate from the free surface into the tissue. It seems to me reasonable to say, that as soon as the epithelium of the surface becomes detached, (that it does so in consequence of increased hyperæmia and exudation, *i.e.*, irrigation, has been previously mentioned,) the tissue, thus denuded, is attacked by the vegetable parasite, which, in consequence of its growth, produces a more or less total destruction of the elements of the denuded surface.

I have to draw attention to one other point, viz. the oblong and rounded pits of the ileum, which being surrounded by an elevated wall of mucous membrane, are all generally taken to be ulcers, the slough of which has become detached. On careful examination, however, it is found that this is not the case. On section, a solitary or a small Peyer's gland is occasionally seen, the surface of which has not yet broken down, *i.e.*, is not yet a slough—at any rate it is not yet an ulcer from which a slough has become detached—and which forms the bottom of a roundish or elliptical pit, bordered by thickened mucosa; this latter may, just as in a true ulcer, form almost overhanging lips to that pit. That is to say, on naked-eye inspection, such a place looks like an ulcer, although microscopical examination proves that it has not yet become one (*see* Fig. XXXIX.). The elevated wall of mucous membrane is of rather firm consistence; its blood-vessels, especially those of the thickened submucous tissue, are very much distended.

8. *Changes in the Mesenteric Glands and Spleen.*

As has been correctly described by previous observers, the mesenteric glands show changes in the gland-substance itself and in the capsule. The blood-vessels of the latter are found to be distended, and in its connective-tissue there are large cells in groups and isolated, perfectly identical with those described in the intestine.

The afferent lymphatics are distended, and contain in the earlier stages a finely granular material, a various number of bright spheres in all respects identical with those found in the intestine (*see* Fig. LVII.), and large lymph cells. These are either enlarged lymph-corpuscles, with one large generally constricted nucleus or two nuclei, or, besides their own nucleus, they contain in their substance or in a central vacuole one or more spherical deeply-stained small nuclei. Many cells are found in a state of disintegration.

All the blood-vessels of the gland itself are in a distended condition, and some are filled with blood. The capillary vessels of the follicular tissue of the cortical, as well as of the medullary part, are also much distended, and many of them are provided with local dilatations; they are generally not filled with blood. There is an interesting circumstance connected with their endothelium, viz. that the endothelial membrane in many capillaries and capillary veins is seen to be detached, for a longer or shorter distance from the adventitia, *i.e.*, the supporting matrix; in Fig. LVIII. this condition is well shown.

As regards the mesenteric glands, I am also of opinion, in opposition to other authors, that the stroma of the adenoid tissue, is not hypertrophied in the earlier stages, but is rather rarified. (The adenoid reticulum is here, not a network of fibres, but a honeycomb of membranes, similar to that of the lymph-follicles of the intestine.) In a later stage, when the glandular substance has become yellowish and rather firm and brittle, the adenoid stroma in many places, when examined under the microscope, is seen to be in a necrotic condition:

i.e., it consists of a large number of rather stiff fibrils, interlacing in a very complicated manner; the lymph-cells of these places are gradually fading away (*see* Fig. LV.).

The lymph-sinuses, those surrounding the cortical follicles, as well as those around the medullary cylinders, are more or less filled with lymphoid cells of different sizes, from ordinary small lymph-corpuscles with a single nucleus, up to extremely large cells with a number of nuclei situated in a large vacuole of the cell. The larger lymph-corpuscles, (*see* Figs. XLIX. and LI.) are found chiefly in the lymph-sinuses, especially in those of the cortical part; hence it is probable that many of them have been carried into the mesenteric gland from the intestine. But there are undoubtedly numerous such cells to be found in the adenoid tissue of the cortical, as well as of the medullary part; so that Grohe and Hoffmann are perfectly correct in opposing Billroth, who maintains that they have all been brought into the gland from outside. Indeed, the best examples of the large cells I have seen among the cells of the adenoid tissue. Larger cells, although not those of the largest kind, are contained also in venous vessels, a fact also repeatedly noticed in the intestine. In Fig. LII$^{ii}_{f}$ I have represented as accurately as possible all the more characteristic forms of these cells.

A careful study of these forms (compare the explanation of the figures), will enable the reader to understand why I maintain that the final result of the changes in the cells is the endogenous production of small lymph-corpuscles; that is to say: lymphoid cells, whose substance and nucleus has greatly enlarged, take up small lymph-cells, the nuclei of which become the nuclei of the cells of the new brood which originates in the enlarged corpuscle; this latter is gradually converted into a vesicle filled with nucleated cells, and eventually bursts and discharges the young brood (*see* Fig. LII$_{i}$.).

The chief reason why I regard the small cells and nuclei contained in many of the large cells as not being directly derived from the original enlarged lymph-corpuscle, is because the nucleus of the latter may be recognized almost unchanged up to the period when the vesicular or signet-ring stage has been reached, thus making it quite improbable that the nuclei of the brood are offsprings of the nucleus of the mother-cell. It seems to me to be more a matter of hatching than of originating. In saying this I do not of course deny that small cells may be produced directly from the enlarged ones, as there certainly are examples in which the nucleus shows distinct signs of division, and others in which it has divided into two or three small nuclei. In examining the medullary part of lymphatic glands from the end of the second week of the disease, I find that those cells which stretch across the lymph-sinuses have undergone inflammatory changes, having become very much enlarged; they are, however, still recognizable as more or less flattened cells (*see* Fig. XLIX.). The fibres along which these cells are situated in the normal condition, are broken down; in many places they have altogether disappeared from the lymph-sinuses of the cortical as well as of the medullary part.

Besides the organisms mentioned previously as occurring in the afferent lymphatic vessels, I find also in the proper glandular substance masses of micrococci, always in connexion with the necrotic change of the tissue. Thus I find occasionally a necrotic focus in the cortical follicular tissue, next the lymph-sinuses, containing masses of micrococci (*see* Fig. LVIII.). (The peripheral portions of the cortical follicles, *i.e.*, the portion next the lymph-sinus, are favorite situations for the first commencement of necrotic changes.) I also find in necrotic parts around a blood-vessel, in whose wall a deposition of the dark-coloured material mentioned in the preceding chapter, had taken place, (*see* Fig. LIII.),

masses of micrococci, as well as the larger bright spheres which resist caustic potash, as mentioned when speaking of the intestine; and, finally, I find in some capillary branches regular plugs of dark masses of micrococci (*see* Fig. LIV.).

We come now to the spleen, of which organ I have to state only a few of the earlier changes; these refer chiefly to the condition of the arterial vessels and to the cells found in the pulp. With regard to the first point I can be very brief, having treated of a similar subject already at the occasion of the intestine. The reader doubtless remembers the description of the peculiar changes of the walls of the ultimate arterial branches of the lymph-follicles of the intestine in the early stages of the disease, consisting in the appearance of homogeneous colloid-like masses of a soft substance between the adventitia and inner coat. The same substance is present also in the smaller arterial branches of the spleen; the only difference being that here it occurs in branches, which are still provided with a distinct muscular coat. From Figs. XLVIII$_{i.}$, $_{ii.}$, and $_{iii.}$ it is clear that it produces a distortion, and even a compression of the lumen of the vessel, as in Fig. XLVIII$_{iii.}$ It is also evident from these Figures that the abnormal material does not consist merely in a peculiar change, of the arterial coat, but that it is distinctly due to a deposit between the intima and the middle, *i.e.*, the muscular coat.

As far as I can see, the adenoid sheath of the arteries in general seems to be increased in the earlier stages, and the "capillary sheaths" (Capillarhülsen of Schweigger Seidel) appear also thicker and more distinct than under normal conditions.

The cells forming the pulp, and situated in the distended blood-paths, are chiefly large lymphoid cells; in some places all that is left between the distended blood-sinuses (completely filled with blood), are cells which possess a large nucleus at one point of the periphery, and whose interior is perfectly filled with coloured blood corpuscles; they resemble large blood-cysts. I have represented several examples of this kind of cells. Some of them, the larger ones especially, show among the blood corpuscles, they contain, one or the other spherical deeply-tinted nucleus. All these appearances make it very probable that we have to do with lymphoid cells changed in the same manner as those of the intestine or the mesenteric glands, with the addition that they have had time to take up a great number of coloured blood-corpuscles while slowly passing through the blood-sinuses of the spleen, in which organ the velocity of the circulation is well known to become greatly decreased, even during the earlier stages of the disease. That many of the cells containing blood-corpuscles have passed into the spleen from outside is a matter which needs no special discussion, considering that there is no reason why many of the enlarged lymph-cells, described previously, should not pass from the mesenteric glands, by way of the efferent lymphatics, into the general circulation. Nor is there any reason why similar cells, having passed through the spleen, and having become charged with coloured blood-corpuscles, should not find their way back into the general circulation. The larger veins of the spleen are indeed found to contain large cells, charged with a varying number of coloured blood-corpuscles. I presume the fact that large lymphoid cells filled with coloured blood-corpuscles have been found in the blood of an enteric patient * is to be explained in this manner.

* Eichhorst, Centralblatt, für Med. Wissenschaften, No. 53, 1874.

Fig. I.

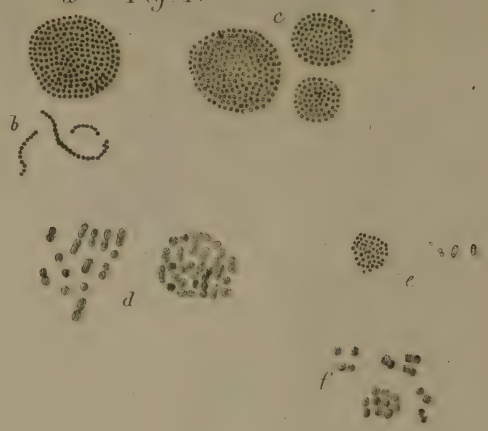


Fig. III.

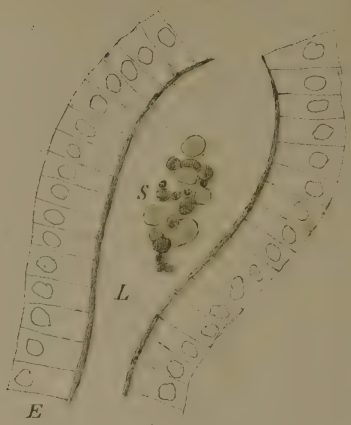


Fig. II.

Fig. IV.

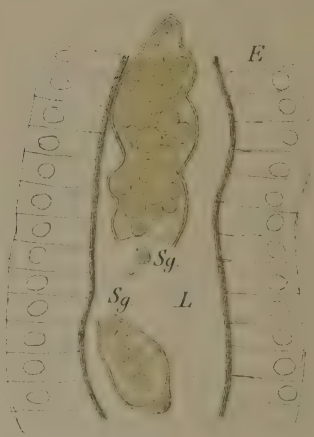


Fig. V.

Fig. VI.

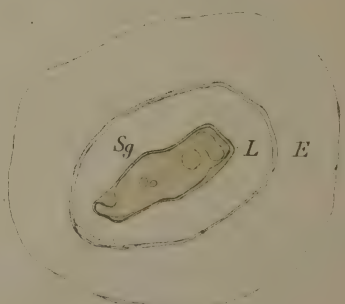


Fig. VII.

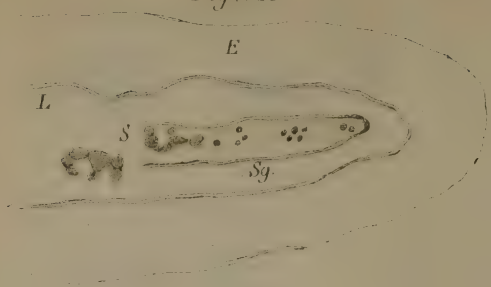


Fig. IX.

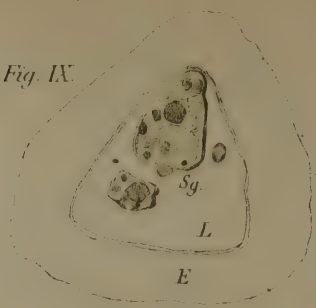


Fig. VIII.

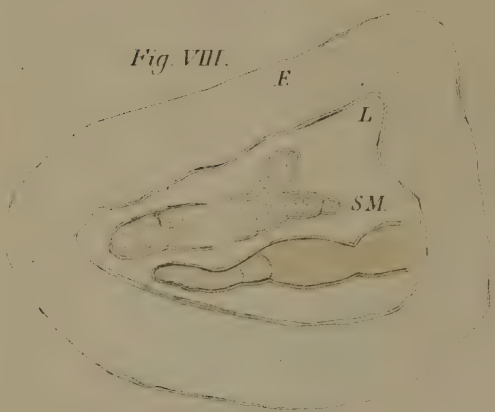


Fig. X.

Fig. XI.

Fig. XII.

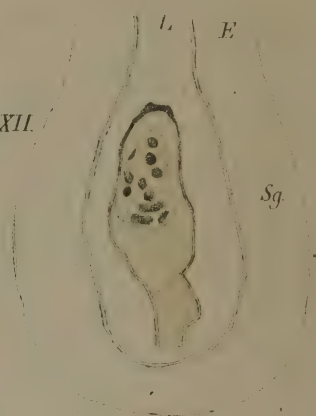


Fig. XIII.

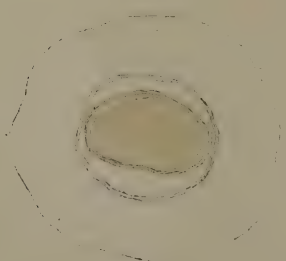
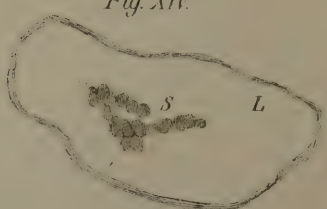


Fig. XIV.



EXPLANATION OF PLATES I. AND II.

In Fig. I. are represented micrococci of fæcal matter of enteric patients.

a. b. c. d. and *e.* from a case in the third week of the disease, *f.* a recent case.
a. From a fresh specimen.
b. From one that had been kept in the incubator for 48 hours.
c. From one that had been kept in the incubator for 24 hours.
d. From the pellicle of a sample of typhoid fæcal matter, which had been kept mixed with water in a closed bottle for about 10 days.
e. From the fluid part of the same sample as *d.*
f. From fæcal matter of a recent enteric case.
a to *e.* Drawn with Hartnack's eye-piece III., Object. 8, (about 400 diam.)
f. Drawn with Obj. 10, à Immers. (about 750 diam.)

Fig. II.—A Lieberkühn's crypt of ileum in longitudinal section.

L. Lumen of the crypt.
S. Spors held together by a transparent interstitial substance.
M. Micrococci contained in lymph-space around the crypt.
A. Adenoid tissue of the surrounding mucosa.
C. Blood-vessels.

Figures III., IV., VII., X., XI., and XII. represent longitudinal sections of Lieberkühn's glands of ileum; the epithelium is left in outline; in all figures is:

E. Epithelium.
L. Lumen of gland.
Sg. Membranous structure containing spores.
S. Spores.
SM. (in Fig. X.) Portion of what is probably the mycelium containing micrococci.

In Fig. IV. the lower of the two bodies marked Sg. is probably a detached goblet-cell (epithelium-cell) containing spores.

Figures V., VI., VIII., IX., and XIII. are transverse sections of Lieberkühn's crypts; the epithelium is here also left in outline. The letters have the same meaning as in the preceding figures.

Fig. XIV.—A blood-vessel (transversely cut) of the mucous membrane of small intestine.

L. Lumen of vessel.
S. Spores.

EXPLANATION OF PLATE III.

FIGURES XV.–XIX. represent blood-vessels containing spores ; the vessels are from the same tissue as Fig. XIV., viz., from the mucous membrane of ileum.

L. Lumen of vessel.
E. Endothelial cells.
S. Spores.

All Figures from II. XIX. (incl.) are taken from specimens obtained of Case I. (see text). They are drawn with Hartnack's E. p. III., Obj. 10, à Immers.

Fig. XV.

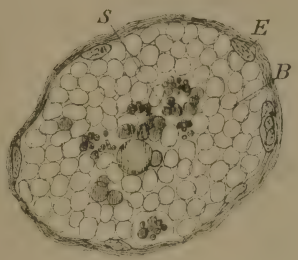


Fig. XVII.

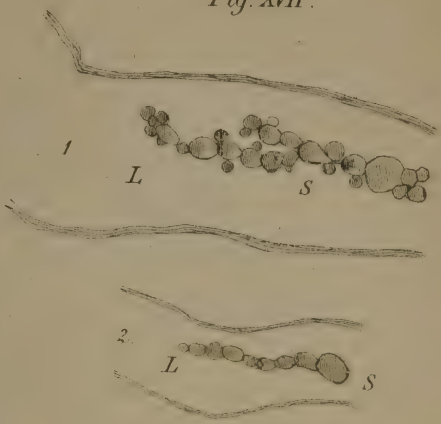


Fig. XVI.

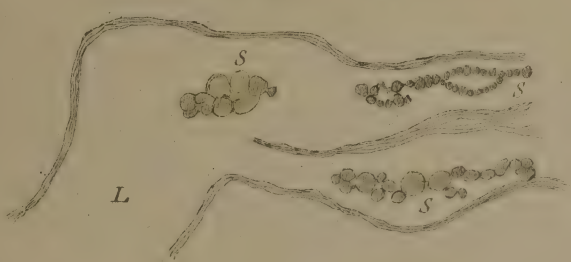


Fig. XVIII.

Fig. XIX.

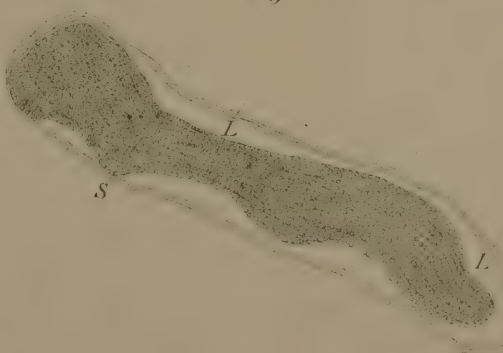


Fig. XX.

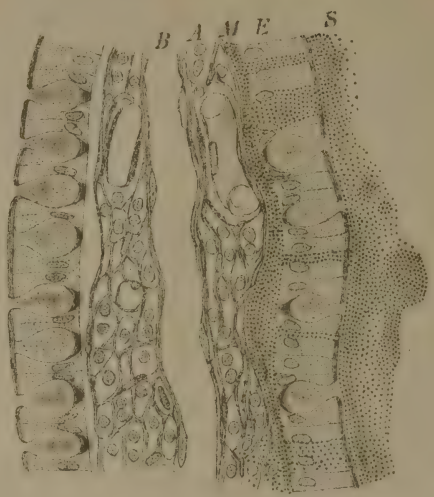


Fig. XXI.

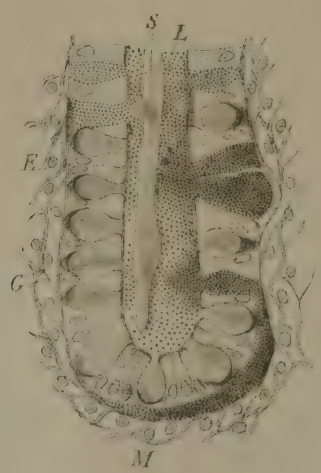
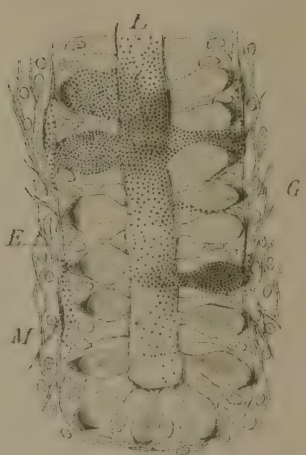


Fig. XXII.



EXPLANATION OF PLATE IV.

FIG. XX.—The greater portion of a villus of ileum (Case II.) cut longitudinally.

E. Epithelium.
B. A blood-vessel.
A. Adenoid tissue containing small blood-vessels.
M. Masses of micrococci accumulated underneath, and within, the epithelium, and also on the free surface *S.*

FIG. XXI. and XXII. are Lieberkühn's crypts in longitudinal section from the same intestine as Fig. XX.

E. Epithelium.
L. Lumen of the gland, containing masses of micrococci.
g. Goblet-cells.
M. Micrococci in spaces around the crypt.
S. In Fig. XXI. a band of mucous.

All three figures are drawn with Hartn. E. p. III., Obj. 7, (about 300 diam.)

EXPLANATION OF PLATE V.

FIG. XXII.—Longitudinal section through a Lieberkühn's crypt of ileum Case III.).

E. Epithelium.
L. Lumen.
M. Micrococci in a space around the gland.

FIG. XXIV.—Transverse section of a Lieberkühn's crypt of ileum (Case I.)

Letters as before.

Hartn. E. p. III., Obj. 8.

FIG. XXV.—From a section through the mucous membrane of ileum in the vicinity of a Peyer's gland (Case IV.)

S. Internal surface of the mucosa covered with micrococci.
E. Epithelium.
L. Lumen of Lieberkühn's crypt.
C. A Lieberkühn's crypt in tranverse section, greatly distended.
M. Sub-epithelial space containing micrococci.
g. Adneoid tissue.
B. Blood-vessels.

Hartn. E. p. III., Obj. 7.

Fig. XXIII.

Fig. XXIV.

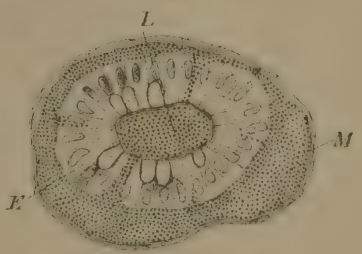


Fig. XXV.

Fig. XXVI.

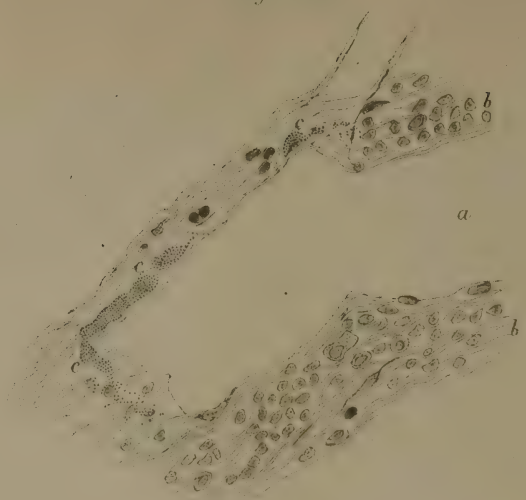


Fig. XXVII

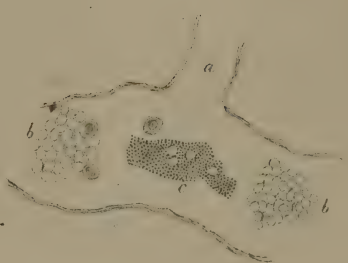


Fig. XXVIII.

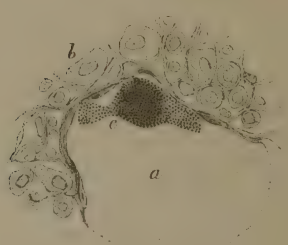
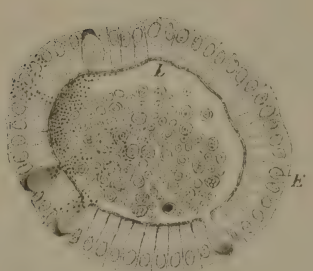


Fig. XXIX.



EXPLANATION OF PLATE VI.

FIG. XXVI.—A vein of the submucous tissue of ileum (Case II.) in the vicinity of a Peyer's gland.

a. Lumen of the vessel.
b. Tissue surrounding the vein.
c. Micrococci.

FIG. XXVII.—From the same specimen as before.

a. Lumen of a vein.
b. Blood-corpuscles.
c. Micrococci.

Both figures drawn with H. E. p. III., Obj. 7.

FIG. XXVIII.—From the same specimen as before, but from the tissue of the Peyer's gland.

a. Lumen of a distended blood-vessel.
b. Adenoid tissue around it.
c. Micrococci.

Hartn. E. p. III., Obj. 8.

FIG. XXIX.—Transverse section of a Lieberkühn's crypt from the same intestine as before.

E. Epithelium.
L. Lumen containing lymphoid cells and micrococci.

Hartn. E. p. III. Obj. 7.

EXPLANATION OF PLATE VII.

Fig. XXX.—From the mucosa of ileum (Case II.)

m. Muscularis mucosæ.
b. Large blood vessels.
c. Capillaries.
ad. Adenoid tissue.
l. Micrococci contained in spaces which are probably lymphatics.

Hart. E. p. III., Obj. 7.

Fig. XXXI.—Contents of a vein in the adenoid tissue of Peyer's gland at the beginning of ulceration. (From Case V.)

Fig. XXXII.—Represents a vein and a portion of the adenoid tissue adjoining it, of the same specimen as before.

b. Lumen of the vein.
ad. Adenoid tissue.

Fig. XXXII.—From a similar specimen as the preceding figure; treated with caustic potash. The outlines of the lymph-corpuscles are represented by the engraver very much too hard and distinct, in reality their outlines are only just perceptible, the cells having faded considerably. All three figures drawn with Hart. E. p. III., Obj. 8.

Fig. XXX.

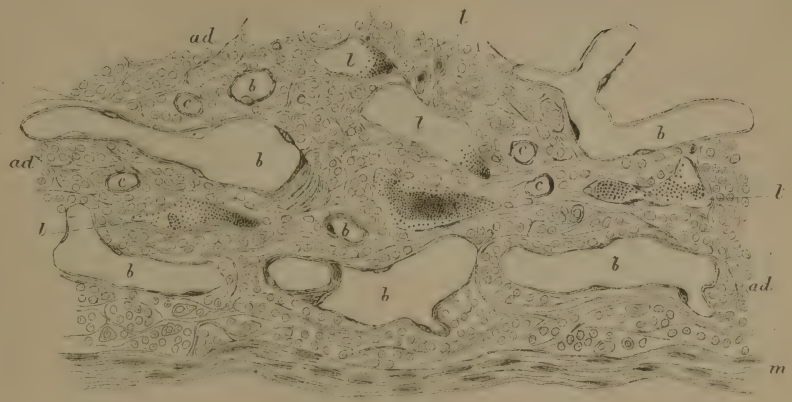


Fig. XXXI.

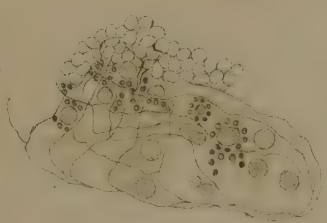


Fig. XXXII.

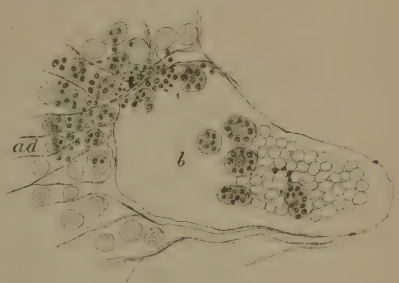


Fig. XXXIII.

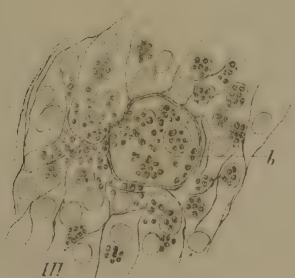


Fig. XXXIV.

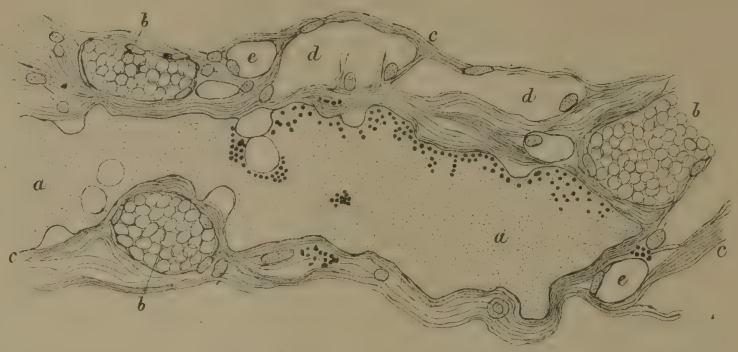
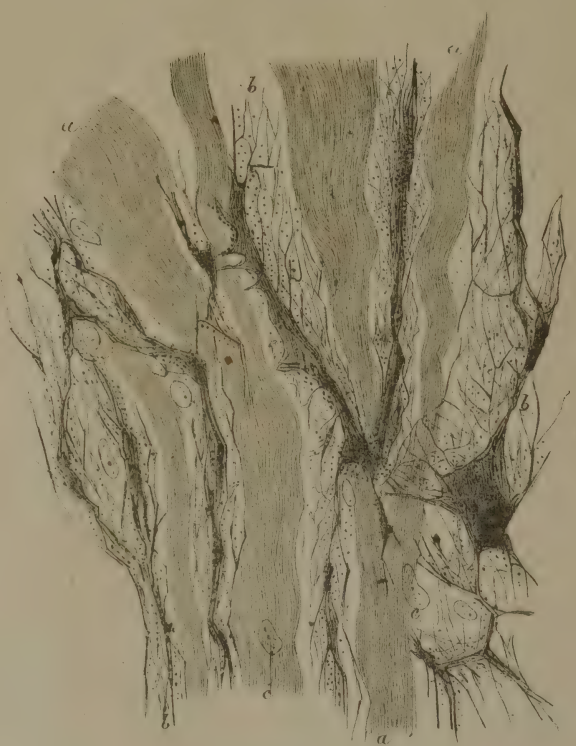


Fig. XXXV.



EXPLANATION OF PLATE VIII.

FIG. XXXIV.—Œdematous submucous tissue in the vicinity of ulcerating lymph-follicles of ileum (Case IV.)

a. A lymphatic vessel containing a uniform granular material—coagulated plasma; in it are suspended highly refractive micrococci, similar organisms are outside the vessel.
b. Blood-vessels filled with blood.
c. Connective-tissue.
d. Distended interfascicular lymph-spaces.
e. Dropsical (vacuolated) nucleated corpuscles.

Hartn. E. p. III., Obj. 7.

FIG. XXXV.—Submucous tissue underneath a swollen Peyer's gland (ileum of Case II.), containing in its distended interfascicular spaces *b* :

a. Peculiar dark material (see text).
b. Connective-tissue bundles (represented very much too hard).
c. Nuclei of connective-tissue corpuscles.

Hartn. E. p. III., Obj. 8.

EXPLANATION OF PLATE IX.

FIG. XXXVI.—From a section through a swollen Peyer's gland of the ileum, (Case II.); the section had been treated with caustic potash.

a. Corpuscles found in the follicullar tissue of the Peyer's gland itself.
b. Similar corpuscles in the mucosa.

Hartn. E. p. III., Obj. 10, à Immers.

FIG. XXXVII.—From a section through a swollen follicle of ileum (Case III.); the section has been treated with caustic potash.

In *1* is represented a network of blood-vessels under a low power (90 diam.); they are filled with micrococci, which are distinctly visible with a high power as in *2* ar d *3*.

2. As seen with 10 Immersion.
3. A seen with Obj. 8.

Fig. XXXVII.

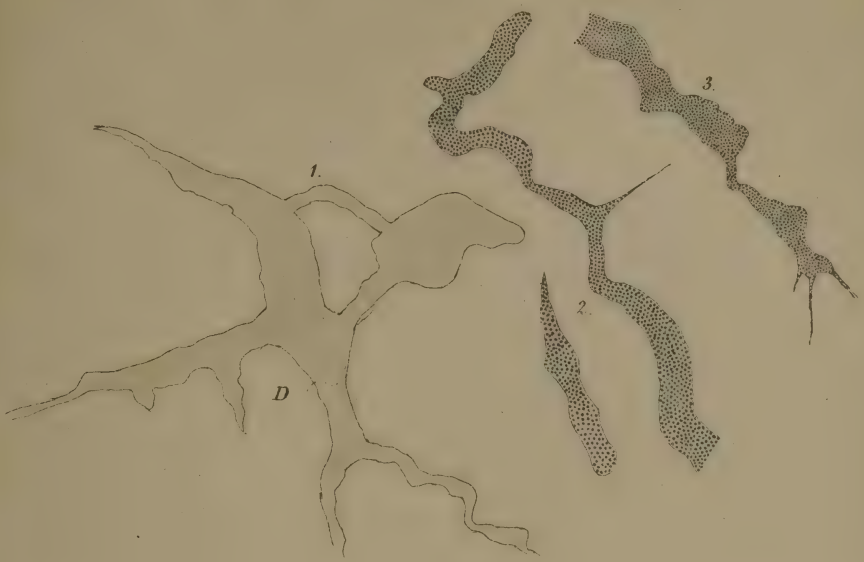


Fig. XXXVI.

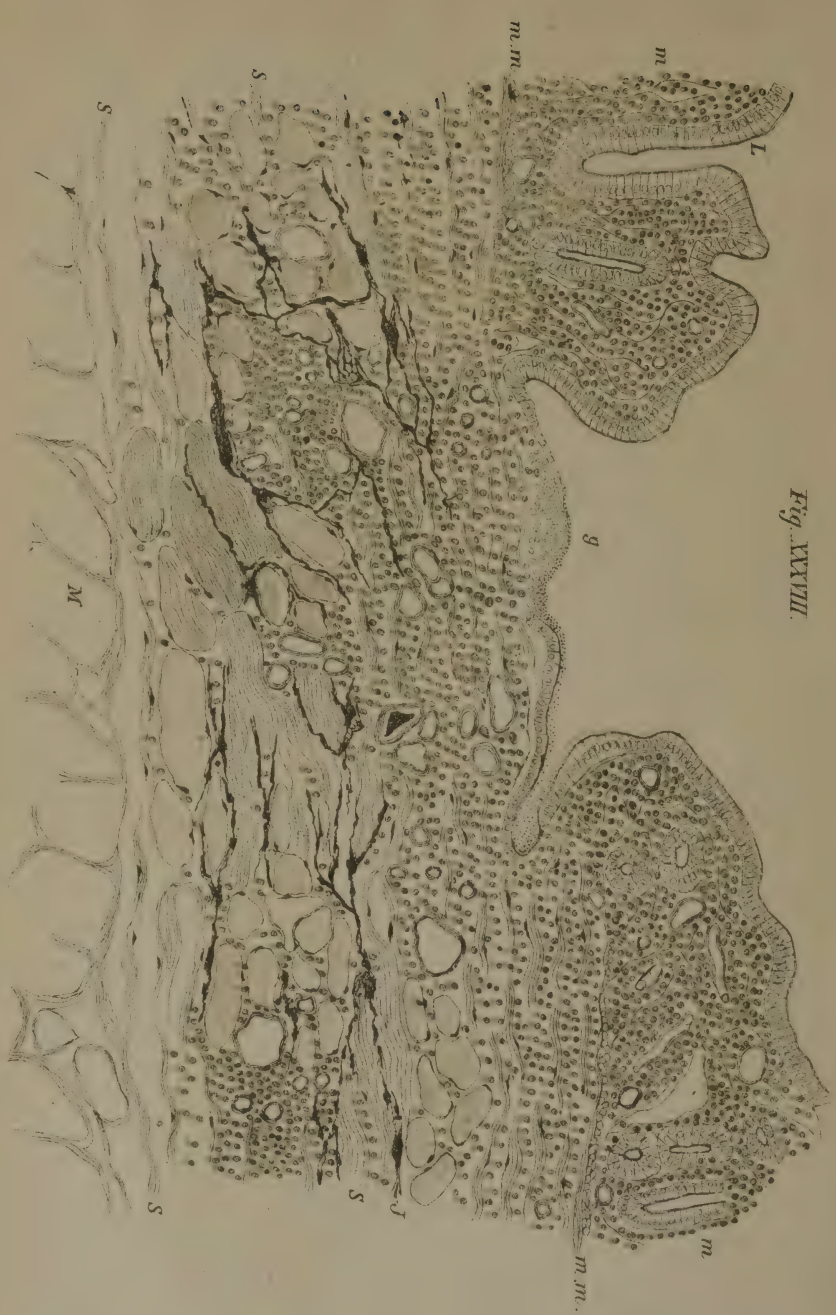


Fig. XXVIII.

EXPLANATION OF PLATE X.

FIG. XXXVIII.—Vertical section through an ulcer (ileum of Case IV.)

g. Bottom of the ulcer, represented by mucosa which is partly denuded of its epithelium; where this is the case the tissue is filled with small round cells (pus-corpuscles); micrococci cover the bottom of the ulcer.

m. Mucosa.

L. Lieberkühn's crypts.

mm. Muscularis mucosæ.

S. Submucous tissue; between its connective-tissue bundles, which are seen in longitudinal and tranverse section, i.e., in the interfascicular spaces J, is contained the peculiar dark material (see text).

M. External muscular coat (not represented).

Hartn. E. p. III., Obj. 4.

EXPLANATION OF PLATE XI.

FIG. XXXIX.—Transverse section through an oblong pit surrounded by an elevated rim of mucous membrane.

a. Epithelium of surface.
b. Villi.
c. Lieberkühn's crypts.
d. Bottom of the pit; the lining epithelium is partly wanting; below it a swollen solitary lymph-follicle.
mm. Muscularis mucosæ.
f. A vessel (lymphatic) filled with opaque material; the same material also in the interfascicular lymph-spaces of the submucosa *S*.
h. Connective-tissue bundles.
g. Veinous vessels filled with blood.

Hartn. E. p. III., Obj. 4.

Fig. XXXV.

Fig. XL.

EXPLANATION OF PLATE XII.

FIG. XL.—From a vertical section through a swollen Peyer's gland of ileum.

P. The most external part of the Peyer's gland; underneath it ordinary connective-tissue *S.*, forming the deepest, i.e., the most external portion of the submucosa.

B. Blood-vessels.

L. Lymphatic vessel; both vessels filled with opaque material; the same is found also in the interfascicular lymph-spaces of *S.*

Necrosis of the tissue of the deeper parts of Peyer's gland has already commenced, its elements losing their distinct outlines, becoming pale and gradually breaking down into an amorphous mass; the matrix of the gland appears in many places to be a dense reticulum of opaque fibres.

Hartn. E. p. III., Obj. 5.

EXPLANATION OF PLATE XIII.

FIG. XLI.—From a section through a swollen Peyer's gland, showing the enlargement of the lymphoid corpuscles of the adenoid tissue.

a. Blood-vessel.
b. Matrix, which is not a reticulum of fibres as commonly described of all lymphatic tissues, but a honeycomb of membranes.
c. Enlarged lymph-corpuscles.
d. Intermediate forms between the former and ordinary lymph-corpuscles *e*.

Hartn. E. p. II., Obj., 10 à Immersion.

FIG. XLII.—From a section through a swollen Peyer's gland, showing further enlargement of the lymphoid cells, the membranous matrix having at the same time given way to large protoplasmic masses.

a. Blood-vessel.
b. Lymphatic space around it.
c. Protoplasmic masses of more or less indistinct outlines and containing nuclei.
d. Lymphoid corpuscles.
e. Lymphoid cells very much enlarged and containing numerous bright nuclei and small cellular elements.

Hartn. E. p. III., Obj., à Immersion.

Fig. XLI.

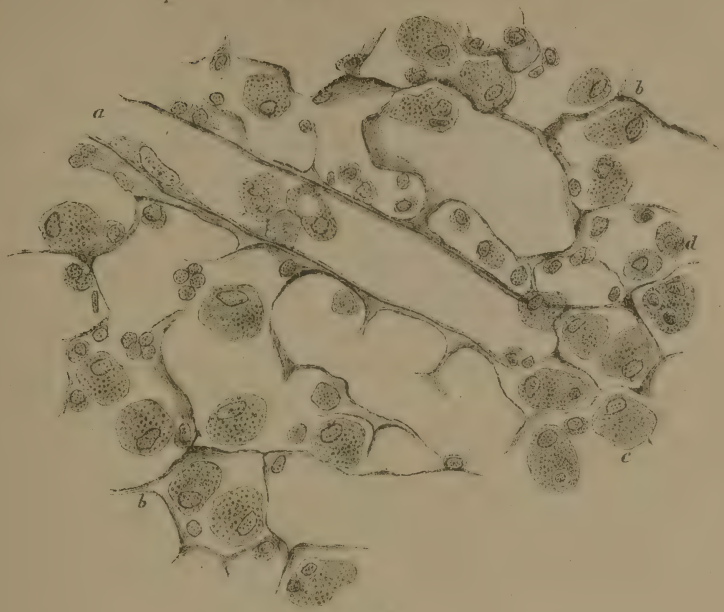


Fig. XLII.

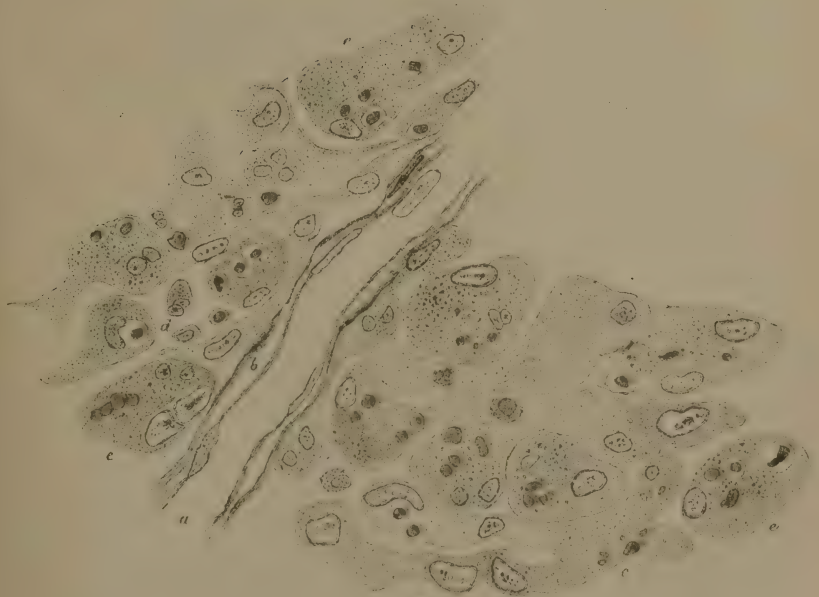


Fig. XLIII.

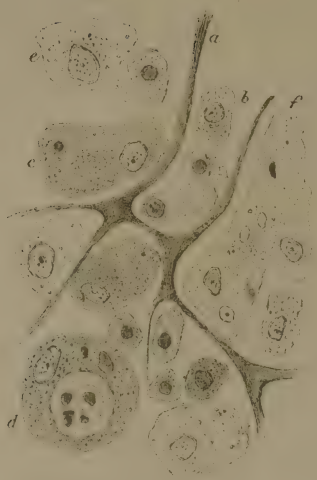
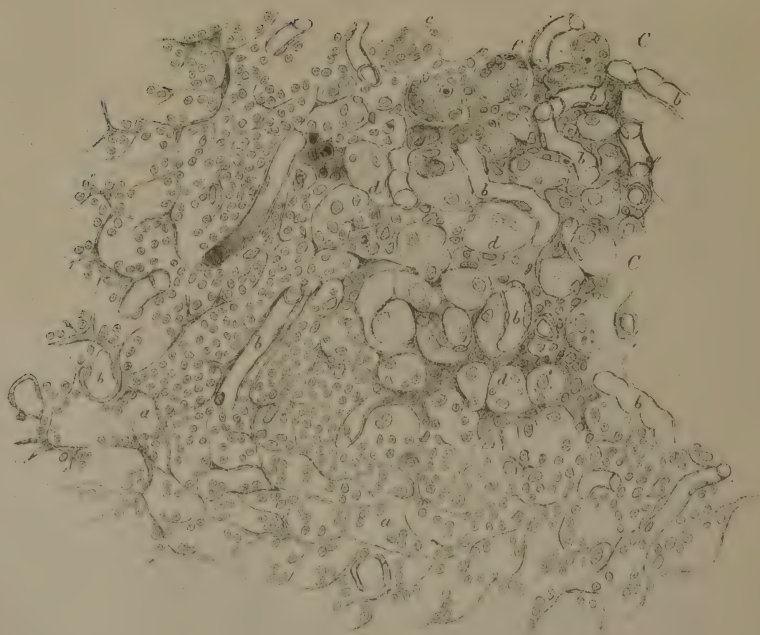


Fig. XLIV.



EXPLANATION OF PLATE XIV.

FIG. XLIII.—From the same preparation as Fig. XLII., showing similar changes in the mucous membrane.

a. Membranous matrix.
b. Pale transparent small lymphoid corpuscles.
c. Opaque lymphoid cells, much enlarged.
d. Enlarged cell containing in a vacuole several small nucleated elements.
e. and *f.* Large pale flattened endothelial-like cells.

Hartn. E. p. III., Obj. 10, à Im.

FIG. XLIV.—Section through a lymph-follicle of a Peyer's gland of a very early case (Case I.)

C. Centre of the follicle converted into a spongy mass, in which may be recognised blood-vessels *b.*, in connexion with them opaque nucleated trabeculæ *c.*, and spaces each containing a transparent cell-plate *d.*; the peripheral part *a.* of the follicle is adenoid tissue of ordinary aspect, *i. e.* a honey-comb of membranous tissue containing small lymphoid cells (with a low power generally only their nuclei are perceptible,) and large cells with a vesicular nucleus, similar to the cells marked *d.*

At *e.* and *f.* the meshes contain multinuclear giant-cells.

Hartn. E. p. III., Obj. 7.

EXPLANATION OF PLATE XV.

FIG. XLV.—From a similar preparation as Fig. XLIV.

In the centre of the follicle all meshes filled up by giant-cells *b.*; some of these have distinctly a tubular shape; *d.* appears to be a tube cut transversely, *b.* one nearly transversely, and *c.* one cut obliquely; at *e.* the cells lining the cavities.

a. Framework composed of nucleated fibrillar trabeculæ and containing blood-vessels.

Hartn. E. p. III., Obj. 8.

FIG. XLVI, I. and II.—Giant-cells surrounding peculiar foreign bodies, probably vegetable parasites, in a preparation as before. They are found commonly in the submucous tissue, in some instances also in the mucosa (see text).

a. Foreign body.
b. Giant-cell.
c. Transparent flattened cells.
d. Small giant-cells.
e. Connective-tissue wall, appears to be the wall of a vessel surrounding the foregoing structures.
f. Capillary vessel.

Hartn. E. p. 2., Obj. 10, à Immersion.

Fig. XLV.

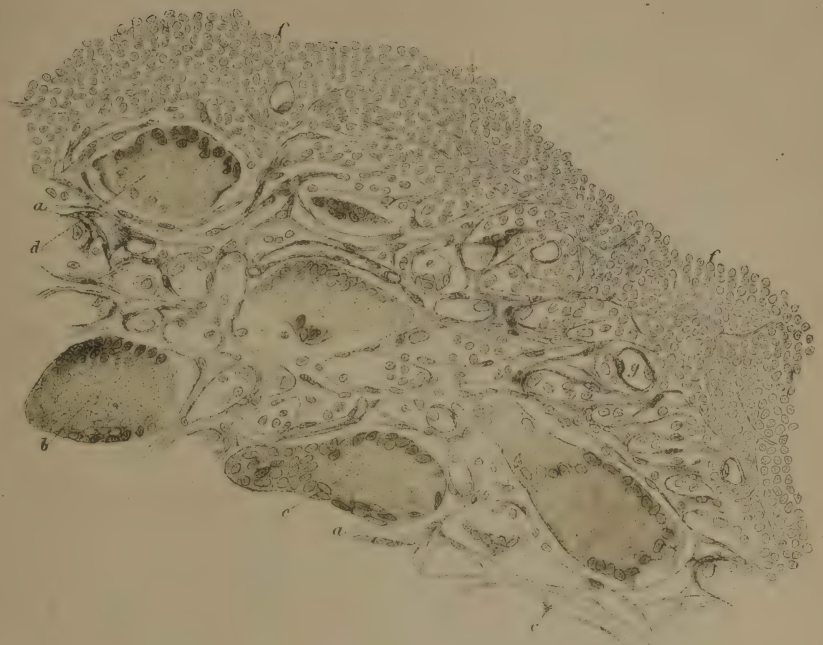


Fig. XLVI

Fig. XLVI

Fig XLVII.

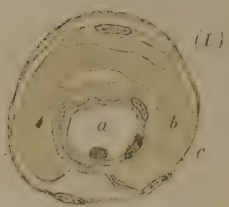


Fig XLVII.

Fig. XLVII.

Fig. XLVII.

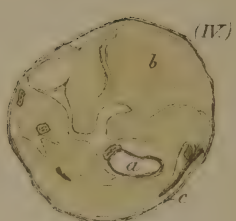
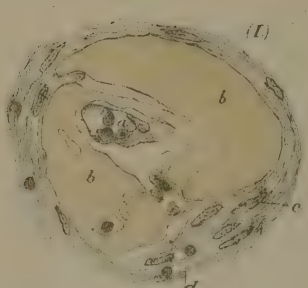


Fig. XLVIII.



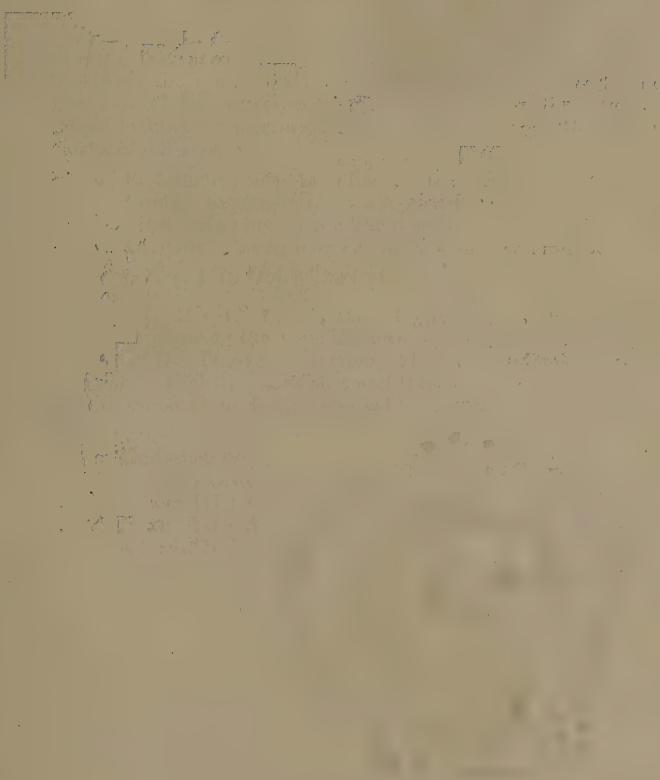


Fig. XLVIII.

Fig. XLVIII

EXPLANATION OF PLATES XVI. AND XVII.

FIG. XLVII., I., II., III., and IV.—From the same intestine as Fig. XLIV. showing transverse sections of blood-vessels (ultimate branches of arteries) from near the central part of the changed lymph-follicles (see Fig. XLIV.) The coat of the vessel excessively thickened by the presence of a peculiar colloid-looking homogeneous material, which is deposited in more or less oblong blocks of different sizes.

a. Endothelial membrane lining the lumen.
b. Peculiar material; in it are spaces to be recognised, which in some instances contain nucleated cells.
c. Adventitia, being here an endothelial membrane.

Hartn. E. p. III., Obj. à Immers.

FIG. XLVIII., I., II., and III.—From the spleen of another typhoid case (Case II.), showing the same changes in the arterial branches.

I. and II. Tranverse section, III. longitudinal section; the peculiar material is slightly yellowish-tinted and has not stained with hæmatoxylin, but otherwise is perfectly identical with that in the vessels of the preceding figures.

a. Endothelium.
b. Peculiar material.
c. (I. and III.) Circular muscular coat. *c*. (II.) Lymphoid cell.
d. (I. and III.) Adventia. *d*. (II.) Circular muscles.
e. Adventitia.

I. and II. are drawn with Obj. 10, à Immers., III. with Obj. 8.

EXPLANATION OF PLATE XVIII.

FIG. XLIX.—From the medullary part of a mesenteric gland (Case V.)

a. Trabecula. In the lymph-sinuses close to it lie *b*. large cells, probably the branched cells found in them in the normal condition, only here much enlarged.
c. Lymphoid-cells very much enlarged and containing several nuclei.
d. Large lymph-corpuscles.
e. Ordinary small lymph-corpuscles.
f. Vacuolated lymph-cells, containing several nuclei in the vacuole.

Hartn. E. p. III., Obj. 8.

FIG. L.—From the follicular tissue of a similar specimen as before, showing enlargement of lymphoid cells.

a. Honeycomb of membranous matrix.
b. Enlarged lymph-corpuscles containing in a vaculo numerous nuclei and lymphoid cells.
c. and *e*. Smaller lymphoid elements.
d. Ordinary lymph-corpuscles.

Hartn. E. p. III., Obj. 8.

Fig. XLIX.

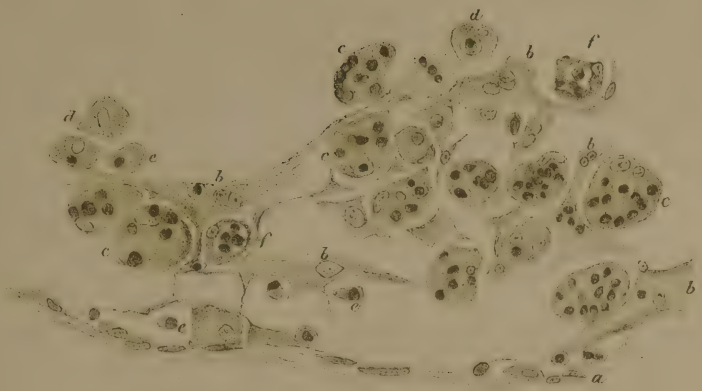


Fig. L.

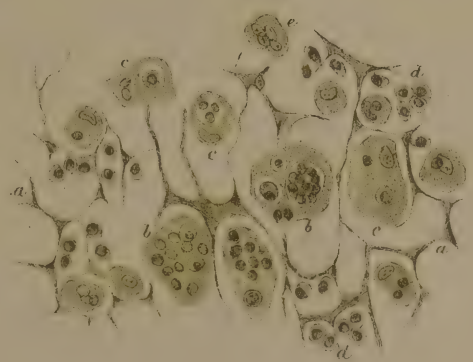


Fig. LI.

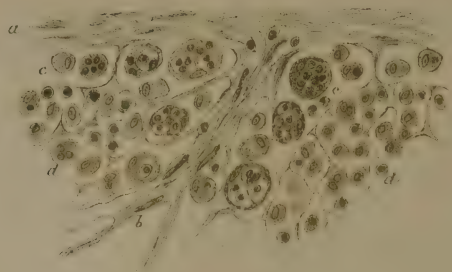


Fig. LII.

Fig. LII.

EXPLANATION OF PLATE XIX.

FIG. LI.—Transverse section through cortical part of the same gland as before.

a. Capsule.
b. Trabeculæ projecting into the depth.
c. Lymph sinuses containing numerous vacuolated cells with many nuclei.
d. Follicular tissue.

Hartn. E. p. III., Obj. 7.

FIG. LII., I. and II.—Vacuolated cells found in the peripheral sinuses of the same preparation as before.

I. shows one such cell that has opened itself, but has not yet discharged its content of lymph-corpuscles.

II. Shows smaller cells of the same kind.

d. Is already broken open.
a. Evidently only one half of a cell, which has become hollowed out, so as to contain a number of cavities separated from each other by thin septa, the residues of the original protoplasmic substance.
The cavities contain lymphoid corpuscles of different sizes (different stages of development), some of which contain even two nuclei as at *b*.
c. and *e*. are apparently younger stages than *a*. and *d*.

I. is drawn with Obj. 10, à Immers.
II. with Obj. 8.

EXPLANATION OF PLATE XX.

FIG. LIII.—From a section through the cortical part of a swollen mesenteric gland of Case II.

a. Blood-vessels distended.
b. Blood-corpuscles.
c. Deposit of opaque material in the wall of the vessels.
d. Adenoid tissue.
e. Detached endothelial cells of the vessel.
f. Beginning necrosis in portions which contain micrococci.

Hartn. E. p. III., Obj. 5. (about 160 diam.)

FIG. LIV.—From a similar specimen as before, showing a distended blood-vessel in transverse section.

a. Lumen of the vessel.
At *b*. Fibrin threads.
c. A block of opaque material in which micrococci may be recognised; this block is evidently extending into a side-branch *c*. obliquely cut away.

Hartn. E. p. III., Obj. 8.

Fig. LIII.

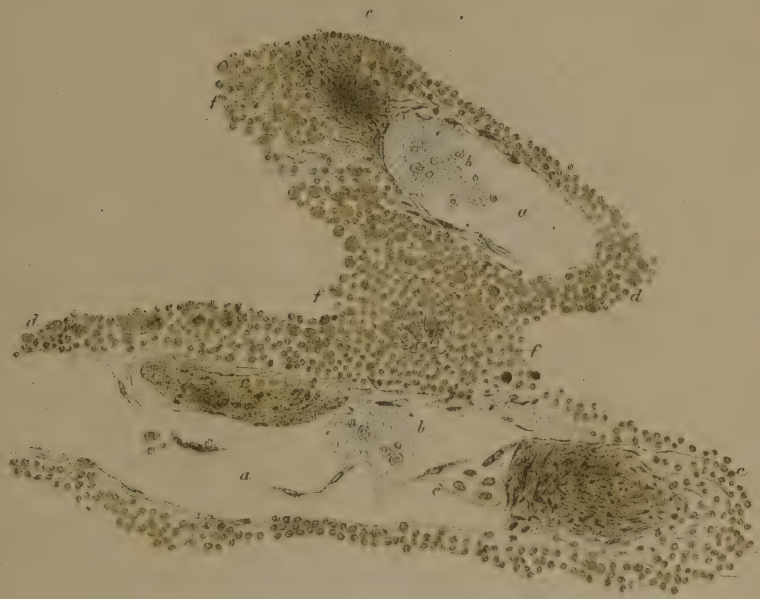


Fig. LIV.

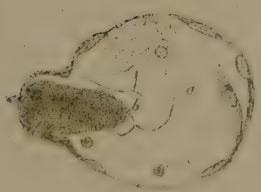


Fig. LV.

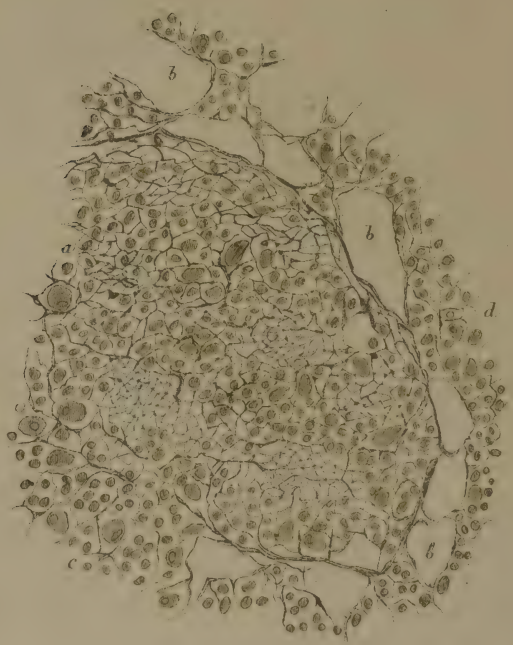
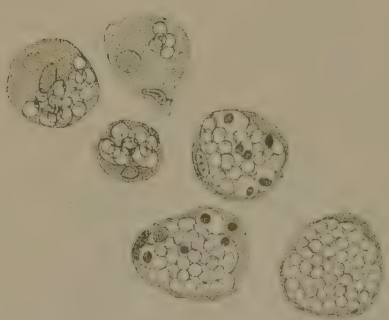


Fig. LVI.



EXPLANATION OF PLATE XXI.

FIG. LV.—From a section through a yellowish brittle portion of the medullary part of the same gland as Fig. LIII.

a. Follicular tissue in a necrotic condition, the cellular elements being very pale, their outlines very indistinct (in the figure very much too sharp,) in many places the lymph-cells have altogether disappeared; the matrix is a very dense network of fine fibrils.

b. Lymph-sinuses.

c. and *d*., part of the follicular tissue in which the lymph-corpuscles have not yet faded.

Hartn. E. p. III., Obj. 7.

FIG. LVI.—From a section through the spleen of Case II., showing large cells of the pulp filled with coloured blood-corpuscles. Drawn with Hartn. E. p. III., Obj. 8.

EXPLANATION OF PLATE XXII.

FIG. LVII.—From a vertical section through the capsule of a swollen mesenteric gland (Case II.)

L. An afferent lymphatic vessel.
a. Arterial vessels.
v. Part of a distended vein.
b. Small lymph-corpuscles.

Hartn. E. p. II., Obj. 7 (about 250 diam.)

FIG. LVIII.—From a vertical section through the peripheral part of the same gland as before.

a. Connective-tissue and lymph-corpuscles of the capsule.
L. Afferent lymphatic vessels.
S. Cortical lymph-sinus.
M. Necrotic portion of the follicular tissue, containing micrococci.
F. Large cells of the follicular tissue.
B. Distended blood-vessel.
e. Its endothelium detached from the supporting matrix.

Hartn. E. p. III., Obj. 7.

Fig. LVII.

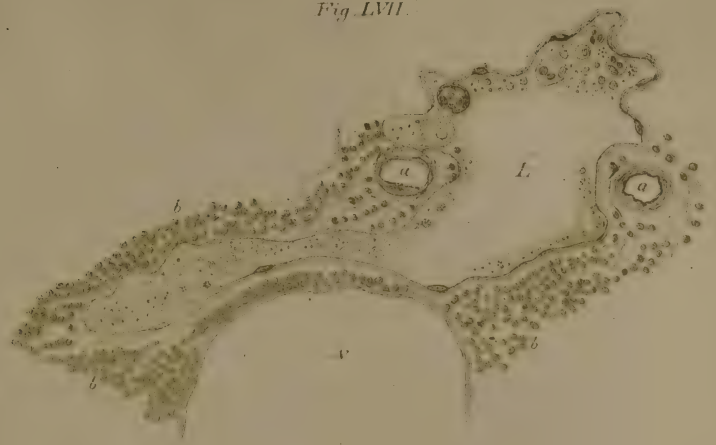
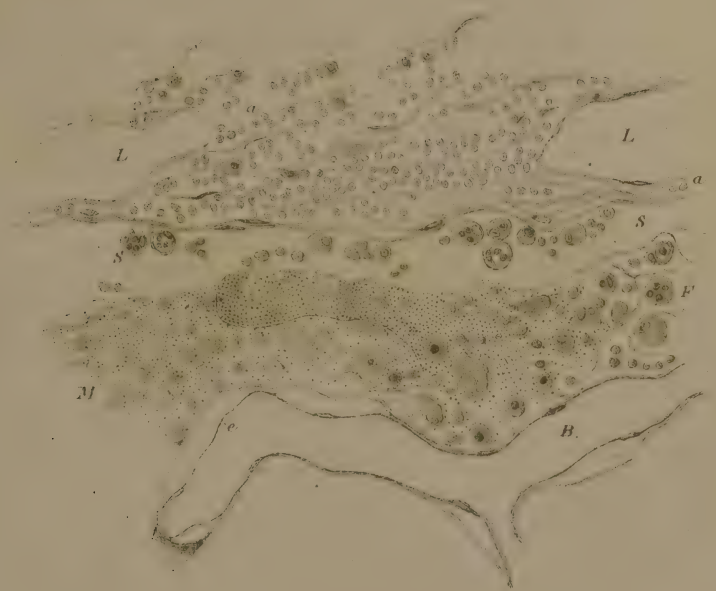


Fig. LVIII.



No. 4.—Dr. Creighton's Report of a further Anatomical Research towards the Ætiology of Cancer.

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Introduction.

The present research is in direct continuation of that published in the last volume of the same reports (New Series, No. III.) One result of the previous investigation—on the histogenesis of secondary tumours in the liver—was to suggest a certain theory as to the origin of primary tumours of epithelial organs, and some progress was made in testing this theory in the case of cancers of the breast. But it soon became apparent that one had to deal with pathological processes for which the existing information on the structure and function of the breast afforded no adequate basis of investigation; and it was hoped that a minute study of the very remarkable and almost unique periodical changes to which the mamma is subject within the child-bearing period would help to supply some of the obvious defects in our physiological knowledge. This expectation has been quite realised. The first part of the report will contain the account of a protracted investigation on the normal processes of involution and evolution of the breast; and in the second part, the facts derived from the study of those processes will be made the basis of an intelligible and more or less sufficient account of the origin of several varieties of cancer of the breast, and of a theory of their malignancy.

Definition of terms.

By the involution of the mamma is understood that regressive process in the breast which follows the conclusion of each period of suckling, and which is accompanied by a marked decrease in the size of the organ. The term evolution is used to denote the corresponding process which precedes the next period of suckling, and which is marked by the well-known increase in the size of the gland towards the end of pregnancy. The investigation will be directed to explain the minute changes, or the changes in the individual cell, which result in the gross decrease or increase of the organ in the respective processes.

Previous applications of the same terms.

Both of the terms here used have been already applied to the mamma in a somewhat different sense. Thus, Sir Astley Cooper, in his work on the Anatomy of the Breast, applies the term evolution to a group of developmental processes, including the first formation of the gland in the embryo, the changes that it undergoes up to puberty, and its complete development in the primipara. The involution of the mamma, in like manner, has been taken to mean that part of general "sexual involution" which affects the breast, and which leads to a final atrophy or disappearance of its secreting structure. It would be difficult, however, to find another pair of words so well adapted to express the periodical changes in the mature breast, and they will be used for that purpose throughout this research. When the developmental processes in youth and the atrophic process at the climacteric period are referred to, they will be distinguished from the periodical processes of the child-bearing period by means of some additional term.

App. No. 4

On the Ætiology of Cancer, by Dr. Creighton.

The extent of previous researches.

The periodical evolution and involution of the breast have not hitherto been made the subject of investigation so much as the developmental processes. The two principal writers on the anatomy of the breast are Sir Astley Cooper* and Professor Langer of Vienna.† In the treatise of the former, the distinction between the periodical changes in the mamma and the changes in youth and at the climacteric period is not closely observed, and there is no account given of minute cellular processes. In the research of Langer, the involution, as above defined, is specially treated of, but in that work also, only those appearances that can be made out with the naked eye or with a low power of the microscope, are satisfactorily described. About twenty years after his first publication, Professor Langer contributed the article on the Breast in Stricker's *Handbuch der Lehre von den Geweben*,‡ but the additions that it contains, whether from his own investigations or from those of others, are inconsiderable, and, in particular, the question of the periodical involution and evolution of the gland is left almost untouched. Since that time, it does not appear to have been taken up by any investigator. The neglected state of this unsolved problem is all the more surprising, as the two processes are found uniformly to present certain broad and unmistakeable features. and to exemplify certain principles in physiology which are of the first importance.

Part I.—Physiological Processes of the Mamma.

The physiological part of the research will contain: (1) an account of the involution of the mamma; (2) an account of its evolution; (3) an account of the function performed by the special lymphatic glands of the mamma in both of those processes; and (4) a preliminary notice of certain points in the development of the gland in the embryo, which illustrate the functional activity of the mature gland.

The animals used for the research have been the dog, cat, sheep, rabbit, and guineapig. Sections have been made from glands that have been hardened in various fluids, and the method of staining by logwood has been almost universally followed.

Section I.—The Involution of the Mamma.

It will be convenient to give, in the first place, some account of the mamma in its state of perfect development and full secretory activity, not with a view to bringing forward any new points, but for the sake of illustrating the changes that follow. The characteristic appearances of a gland well advanced in involution will next be described. This condition of the organ has been found, in the animals above enumerated, to fall between the fourth and sixth weeks after lactation has ceased, and it may be taken to be the resting state of the mamma. The entire series of intermediate changes from the end of suckling to the resting state will then be entered on, and this part of the investigation will afford an opportunity for discussing an important physiological law.

Naked-eye appearances of the fully developed mamma.

During the period of lactation, and for a few days both before and after it, the mamma is found to be a finely lobulated organ, of a pinkish colour, succulent, of uniform consistence, and having generally a greater resemblance to the pancreas than to the salivary glands.

In the dog, cat, and rabbit, the chain of glands extends along each side from the groin to the middle of the thorax; except in one case in the cat (a primipara) the chain of glands has been found to be confluent,

* *The Anatomy of the Breast.* London: 1840.

† Ueber den Bau und die Entwickelung der Milchdrüse, *Denkschriften der Wiener Akademie*, 1852.

‡ Leipzig, 1871.

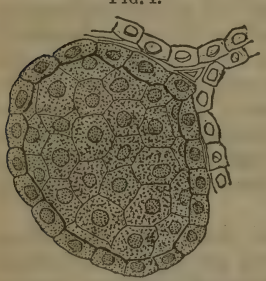
forming a single long strip on each side. In the case mentioned as an exception there were found, corresponding to the five teats, five perfectly distinct circular glands with bands of connective tissue stretching between them. In the general case where the glands are confluent, the same appearance of isolated circular areas is produced by the several sets of ducts (where these are visible) radiating towards each teat.

In the dog, cat, and rabbit there are from four to five teats on each side, in the sheep there are two pairs, a large and a small, and in the guineapig there is a single pair. In the animals that have the extended chain of glands, the anterior two-thirds of the chain is flat and thin, being about two inches in width, and a line or more in thickness; towards the inguinal region the gland becomes much narrower and thicker, and tapers to a rounded point at the symphysis pubis. The upper surface of the gland is closely adherent to the skin throughout; the lower surface is separated from the abdominal wall by a thin layer of loose connective tissue in the anterior part of the chain, and in the inguinal region by a cushion of fat of variable thickness. Small bundles of striped muscular fibre are met with at various points in the gland, running in a longitudinal direction. Their occurrence is, however, not uniform, and there is no regularity in their distribution; they have the appearance of being detached bundles of the subjacent muscle which have, by some means or other, become included in the gland substance.

General account of the minute structure of the fully developed mamma.

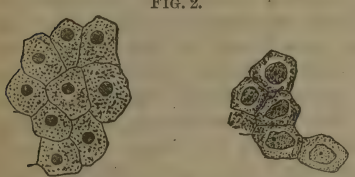
In the minute structure of the fully-developed gland, the following points are to be noted. Each lobulus is composed of a large number of closely packed acini, for the most part of round shape and uniform size, while those at the borders or corners of the lobule may be larger and elongated. The lobules are separated from one another by very thin tracts of loose connective tissue; the acini making up a lobulus are bounded by the encircling blood vessels and their adventitia. The grouping of the acini round the ducts cannot be made out in sections of the fully-developed gland. The floor of an acinus in section is covered by a mosaic of polyhedric epithelial cells, usually to the number of 15 or 20, while in the larger elongated acini as many as 30 may be counted. The cells are usually pentagonal or hexagonal, and the corners are seldom rounded. In each cell there is a central round nucleus which colours brightly with the staining fluid (purple with logwood), and a broad fringe of protoplasm which retains a greyish appearance. The nucleus is on an average not more than one third of the entire breadth of the cell. Fig. 2 shows a variation in the size of the nucleus relative to the surrounding protoplasm. In a profile view of an acinus, the epithelium appears as a circlet of oblong cells in which the nucleus at the centre occupies almost the entire thickness of the cell. The mammary epithelial cell may therefore be described as a flattened polyhedric body, with a thickness about one half of its breadth. The substance of the nucleus is apparently homogeneous, with a deeper line of staining round the margin, but for the most part showing no nucleolus. The broad fringe of pro-

Fig. 1.



Fully developed acinus of the mamma, showing mosaic of polyhedric epithelium. Magnified 300 diameters.

Fig. 2.



Mammary epithelium, showing variations in the relative amount of nucleus and cell substance. Magnified 300 diameters.

toplasm is more or less granular or homogeneous, varying according to conditions that do not require to be discussed at the present stage. By special methods of preparation the meshwork of the basement membrane may be demonstrated. It is seen to be a very regular arrangement of delicate fibres of uniform thickness, forming polyhedric spaces in which the epithelial cells are set. It may be added that the best preparations of the perfect mammary epithelium are obtained, not when the animal is in milk, but two or three days before parturition.

Naked-eye appearances of the involuted mamma.

Turning now to the description of a gland well advanced in involution, the extent of the changes that constitute the involution process will become at once apparent. The entire chain of glands is considerably reduced in thickness, and the anterior end of the chain so much so as to be quite membranous. In the thinnest part of the chain, the ducts, which are not to be seen in the state of full development, are now seen as large round cord-like structures radiating from the periphery to the nipple. The inguinal portion of the chain now rests on a thick cushion of fat; in certain cases this cushion has been found to be three-quarters of an inch or so in thickness, while the gland tissue was, as it were, a mere covering drawn over it. The cushion of fat is also observed to contain small lymphatic glands embedded in it. On cutting into the gland thus reduced in thickness, its substance is found to be tough, and to consist of large tracts of not very dense fibrous tissue, interposed between small round or linear areas of the involuted glandular tissue. The latter have the usual colour and the soft or parenchymatous section of glandular substance, and in the plane of section they incline to stand out slightly above the level of the fibrous stroma. In the greatly flattened or spread-out kinds of glands, as in the dog, cat, and rabbit, the longitudinal section has a stratified appearance, from the arrangement of several involuted lobuli in a long narrow strip, with corresponding parallel tracts of connective tissue. In the more compact glands of the sheep and guinea pig, the islands of glandular tissue are more uniformly scattered over the plane of section. It not unfrequently happens that the tracts of connective tissue between the lobules are occupied by fat. Where this is the case, the contrast between the true glandular and the other tissue is very marked, and the stratified or mottled appearance more striking. The glandular tissue might be estimated roughly to make up less than one half of the entire bulk of the organ. The section of the involuted gland shows also numerous large ducts and blood-vessels cut across.

Microscopic appearances of the involuted mamma.

On microscopic examination the ducts and blood-vessels are always conspicuous. In sections of the fully-developed glands they are seldom encountered; but the great retraction of the glandular substance enables them in the involuted state to become prominent. The fibrous tissue, as has been stated, is frequently occupied by fat. There are cases, however, where the tissue between the lobules is purely fibrillar or coarse fibrous, and the greater or less amount of fat seems to follow the individual peculiarities of the animal. The most stricking instance of fat formation occurred in a rabbit. A portion of the mamma, four days after the young were taken away from suckling, was found to have the uniform parenchymatous appearance of the fully-developed gland. When the animal was killed ten days later, the glandular tissue was found to be greatly retracted or involuted, and the involuted lobuli or groups of lobuli to be separated by broad tracts of pure fat tissue. This rapid development of fat in the rabbit agrees with the observations of Toldt and Czajewicz as regards the rapid disappearance and new formation of the fat tissue generally in that animal.*

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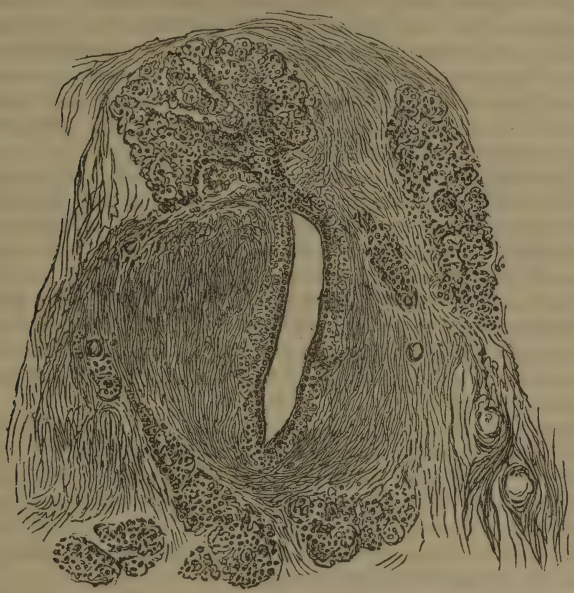
* *Sitzungsberichte der Wien. Akad.*, Juli 1780.

The attention is next directed to the minute structure of the gland tissue proper in the state of involution. The small areas of glandular substance are found grouped with some regularity round the larger ducts. Fig. 3

FIG. 3.



From the mamma of a bitch five weeks after the end of lactation. Characteristic appearance of involuted lobules grouped about a duct. Magnified 90 diameters.

shows a large central duct, sending a branch at its upper end into the centre of a lobule; the other lobules round about it are evidently cut in a plane that does not show the branch of the duct passing into them. The lobule in involution preserves its entirety; that is to say, the acini composing it remain as closely packed together in the involuted state as in the state of full development. There is occasionally found a small growth of connective tissue between the separate acini of a lobule. It is sometimes also observed that the more outlying acini of a lobule are detached from the rest by a few fat cells in cases where fat occurs in the gland. But generally speaking the lobule shrinks up *en masse*, and it is often found that two or three entire lobuli remain closely packed together. The involuted acini present very definite characters, which have been found to occur with great uniformity. Each acinus appears on section as a rounded space bounded by a continuous thin membrane, which generally colours deeply with the staining fluid. It most commonly appears as if the lobule were made up of a number of independent round spaces, but the infundibular or trefoil-like appearance of several communicating acini can sometimes be seen. The diameter of an involuted acinus is about one fourth that of the acinus during lactation. The contents of the involuted acinus are the chief point of interest. Instead of the cellular elements being to the number of 15 to 20 or more, as they are seen

FIG. 4.

Appearance of an involuted lobule with higher magnifying power (300 diameters).

to be in the floor of a perfect acinus, they number, in the sectional view, on the average half-a-dozen; and instead of forming a mosaic of large polyhedric cells of which the central nucleus is not more than one-third of the whole breadth of the cell, they are nothing else than a somewhat irregular heap of naked nuclei, with no fringe of protoplasm round them, and in size little if at all larger than the nucleus alone of the perfect epithelium. The cellular bodies of the involuted or resting state are however not all of them round or elliptical; a certain proportion of them are more oblong, others are crescentic or more or less triangular. They colour with the staining fluid the same as nuclei; the more round or oval forms show a nucleolus.

The involuted acinus is to be regarded as a spherical space more or less completely filled with a number of nuclear bodies. The elements of the basement membrane are not readily made out. There are now and then seen what appear to be spindle-shaped or oblong thickenings in the substance of the limiting membrane; but it is doubtful whether these are not to be classed with the heap of cells within. In like manner there are seen, among the cells in the interior, stellate and other processes which cannot always be distinguished from the crescentic or other irregular forms of cells, which belong without doubt to the general intra-acinous group of cells.

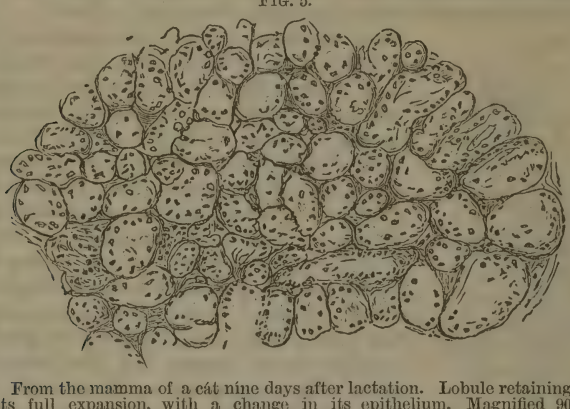
Capillary vessels of a relatively large size can be seen branching in various directions among the acini of the lobule; but they are not seen to encircle the individual acini, as in the state of full development.

Having thus far described the fully-developed state of the secreting structure, and the involuted or resting state of the same, we are now in a position to trace, from the intermediate conditions of the gland, the entire course of the involution process.

The condition of the mamma towards the middle of the involution process.

The adjoining figure is a low-power view of a lobulus from the mamma of a cat that had suckled its young for sixteen days, and had then been kept apart from them for nine days. When the animal was killed at the end of that time, the mammary glands were found little if at all diminished in volume, and to have the ordinary pancreas-like structure of the lactation period. The substance was, however, not at all loaded with milk. On microscopic examination, the lobuli, as the figure shows, were found for the most part to be of the same size as in

Fig. 5.



From the mamma of a cat nine days after lactation. Lobule retaining its full expansion, with a change in its epithelium. Magnified 90 diameters.

the state of full development, and the connective tissue separating them was inconsiderable. The acini also were of much the same shape and size as in the secreting gland, but their contents were totally different. While they retained their size and form, their floor, instead of being

The change in the epithelium of the acini.

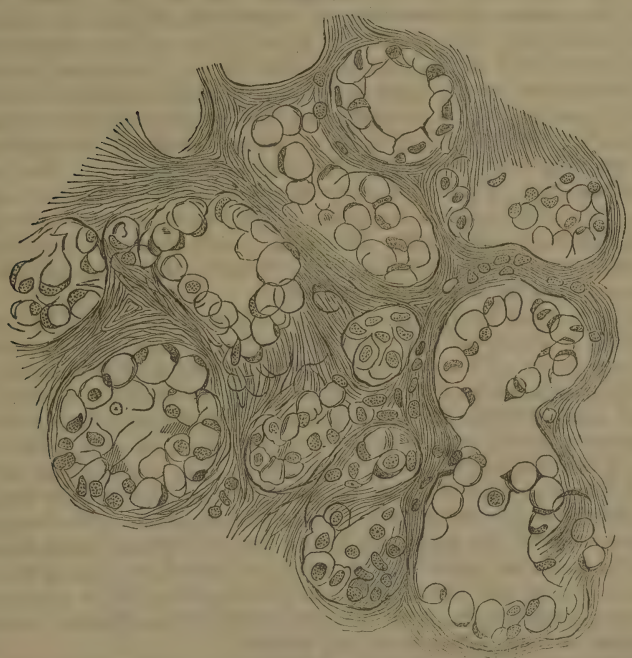
covered with a mosaic of polyhedric epithelium, presented the following appearances, which were characteristic everywhere of the gland structure of this animal. It may be stated also that the appearances were the same in various sets of preparations, whether hardened in chromic acid or in methylated spirit, and whether coloured with logwood or carmine. Each acinus had strewn over its floor, or arranged at somewhat wide intervals round its margin, a number of deeply-stained cellular bodies of various shapes. Some of them were round, some more or less cubical, a certain number were of a somewhat thick crescentic shape (hemispherical), and others were triangular. Their size corresponded generally to that of an epithelial nucleus, and their substance coloured uniformly throughout. It was at the same time apparent that the floor or circuit of the acinus was also occupied by a number of delicate ring-like forms of a greyish unstained granular appearance, and that the variously shaped cellular elements were seated on their periphery (Fig. 6). This was most obvious in the case of the crescent-shaped coloured masses, for they completed the circuit of which the thin uncoloured thread formed the larger part. The triangular shaped bodies were also very significant; they were found situated below the point of contact of two such hoops or rings, a scooped-out side of the triangle forming a part of each circle, and the single triangular body evidently represented the fusion at their opposed surfaces of two independent crescentic bodies.

Fig. 6.

The contents of the acini in Fig. 5 under a higher magnifying power (300 diameters).

The interpretation to be given of these appearances will be made less doubtful by describing what is found in a somewhat different preparation of which Fig. 7 is a drawing. This is from the udder of a

Fig. 7.



From the udder of a ewe shortly after the end of lactation. Vacuolation of the epithelium *in situ*. Magnified 300 diameters.

ewe obtained from the slaughter-house and stated generally to be a short time after the cessation of the milk. The acini were generally of a large size, and their contents showed several interesting modifications of the condition observed in the preceding case. The sections showed more frequently the profile view of the epithelium, in which the cells were arranged as a complete circlet adhering round the circumference of the acinus; and many acini showed, in addition to the circlet of epithelium *in situ* an irregular heap of cells lying free in the lumen of the acinus.

The portion of the gland of which Fig. 7 is an accurate drawing did not show the latter condition, but the group in Fig. 8 are representative forms of the cells that are frequently seen to occupy the lumen of the acini in other parts of the preparation. The cells *in situ* are vacuolated cells, with the usual thin and for the most part uncoloured hoop or ring of the vacuole, and the deeply-stained peripheral mass. The most definite and unmistakeable form of vacuolation is the signet-ring type, which occurs over and over again in these preparations. Another not uncommon appearance, which would be ambiguous if taken by itself, is where the coloured or nuclear element of the epithelium is, to use the current expression, set free from the parent cell, which is evidently not destined to survive the setting free of the young cell. In those cases the definite boundary of a vacuole and the excentric position of the coloured mass are not apparent, but the phenomenon is one of the same class. In the groups of cells that are found lying free in the lumen of an acinus, the process of excavation or vacuolation of the cell substance is very obvious. The cells are true hollow spheres, showing the entire cavity, and not merely a section of it. Individual instances may be observed among them in which the cell substance is seen to be simply granular and not vacuolated; but in these also the excentric position of the nucleus can be seen. Others, again, of the group are round granular cells, showing neither nucleus nor vacuole. The size of the various cells, whether of those *in situ* or of those in the free cavity of the acini, will be found to correspond on the whole to the size of the perfect mammary epithelium. If the latter were to become globular and to retain their greatest breadth as their diameter, they would have much the same size as the cells now described.

Fig. 8.

Characteristic appearance of cells occupying the cavities of the acini in an early stage of involution. (From the same case as Fig. 7.) Magnified 300 diameters.

There is thus a gradual transition from the perfect mammary epithelium to the forms that characterise the various stages of the involution process. The two cases that have been described and figured are merely good examples of what is found uniformly to occur. The various characteristic appearances in the epithelium are found to occur throughout a period extending to the fourth or sixth week after lactation. If the cellular elements of the acini in Fig. 6 are again referred to, it will be seen that they are not unlike those described for the completly involuted or resting state. The remaining steps of the involution process as regards the acini may in the meantime be supposed to be the contraction of the space of the acini as figured in Fig. 5, and the retention of a certain part of the cells within them. This account will have to be supplemented later by some important particulars, but it is convenient to leave it at present as it stands.

Provisional account of the completion of the involution process.

The ultimate contraction of the circuit of the acini evidently depends on the collapse or yielding of the vessels that encompass it, and make

up the most substantial part of its framework. This, again, depends on the diminished supply of blood required by a subsiding secretory activity. As the acini contract they preserve, as has been already said, the unity of the lobule, and it is not between the several acini, but between the several lobules, and sometimes groups of lobules, that a space is set free. There is, as has been explained, an absolute shrinking up of the whole of gland. But there is also an increase of the connective tissue between the lobules, which goes on *pari passu* with the retraction of the latter; and where there is no actual increase in the quantity of the interlobular tissue, there is a formation of fat in it. The production of young fat cells among the interlobular fibrillar tissue is often to be seen. The increase of the cushion of fat beneath the gland has already been mentioned. The economy of this process of fat production is obvious. By means of the sub-mammary layer of fat, the contour of the body is preserved, and by means of the fat within the gland the necessary intervals between such permanent structures as the large ducts and blood-vessels are filled up. In both situations there is the greatest amount of space occupied by employing the least number of cellular elements. Finally the fat tissue is easily removeable when the gland again undergoes its evolution.

The changes in the interlobular tissue.

Such then is the process of involution in the epithelium and in the other tissues of the mamma in so far as its morphology is concerned, or in so far as the objective description of its various phases can carry us. It remains now to enter on a discussion of the physiological significance of the process.

The epithelium of a mammary acinus examined while the animal is in milk is found to be coarsely granular; but it is not always easy to find good examples of the perfect epithelial cells where the formation of milk is actively going on. The character of the epithelium, as has been already stated, can be best seen in the gland shortly before parturition. It is generally admitted that the milk is formed at the expense of individual epithelial cells, and that the epithelial cell perishes in being transformed into the fluid of the secretion. There is, indeed, an observation of Stricker's, which is taken to show* that the same epithelial cell may yield successive contributions to the secretion. He observed that colostrum cells swimming in fresh milk gave out fat globules, while they retained their form. The observation as far as concerns colostrum cells is no doubt correct; but it is at the same time clear that the same colostrum cells could not return to their place on the wall of the acinus and resume their function of milk-production. Whatever properties they may have had as free cells, their career as epithelial cells was over. The cells in Fig. 8 are identical with colostrum cells, and it has been already mentioned that they occurred in the lumen of acini, the walls of which were also covered with a set of epithelium, the colostrum cells being in fact the predecessors of those that then had the epithelial position. It may, indeed, be taken as settled that the secretion is produced by the transformation of the substance of epithelial cells and the necessary destruction of the latter. This process means no less than the constant renewal of the epithelium; and here we are met with a difficulty. The mammary epithelium is an epithelium of one layer, and there is no doubt a difficulty in representing to the mind the double process, the secretory process and the formative process on which it depends, as taking place in an epithelium of one layer. The type of the secretion is, however, the same as in the sebaceous glands, and the latter again are mere modifications of the epidermis. Now, in the latter, the numerous layers of cells enable the process to be clearly seen. In the lowest layers there is a multiplication

During lactation there is a constant renewal of the epithelium of the acini.

Illustration from the *rete mucosum* and epidermis.

* Langer, *Stricker's Handbuch*, p. 632.

of cells by the ordinary hyperplastic process of division; a layer of cells that have begun their career in this manner as formative or plastic cells come in their turn to the surface, and undergo the horny transformation, after which they are cast off. There is here no special class of cells which are set apart for formative activity; the same cells are at one time in a formative stage and at another time in their functional, and the many layers of the cells enable us to see the two incidents of their life apart. The difference in the mamma is that there is visibly present no new generation of cells in readiness to take the place of those that are cast off, but that difference entirely depends on the epithelium being an epithelium of one layer. The same cycle which is, as it were, unrolled in the *rete mucosum* and epidermis, is implicitly present in the activity of the mammary epithelium. With this explanation, it will be convenient to separate the notions of the formative and of the functional activity of the epithelial cells, the latter constantly presupposing the former.

The secretion then may be said to be produced by a transformation of the substance of successive generations of epithelial cells, and in the state of full activity this transformation of the substance is so complete that it may be called a deliquescence.

The process in the cells presents in fact no morphological characters whatever. But when the secretory activity of the gland is weakened, as in the subsidence of the function during involution, the morphological characters of the process become apparent. Reverting to the appearances of the early stage of involution, as in Fig. 7, it will be seen that the process in the epithelium is one of vacuolation. The substance of the cell is transformed into a cavity filled with a fluid, and a certain portion of the cell's substance remains as the wall of this cavity and as a peripheral mass, which colours like the original nucleus. Now, among vacuolated epithelial cells, there will be observed considerable differences in the bulk of this peripheral mass and in the thickness of the wall of the vacuole. In some cases, the former is a large cellular element, as in some of the cells of Fig. 6, in others it is a thin crescent-shaped line, which is distinguishable from the rest of the vacuole outline only by its property of staining. Cells of this variety may be seen *in situ* in Fig. 7. We are here in the midst of a series of gradations. In the vacuolation process there is evidently a correlation between the amount of the cell substance that is devoted to the vacuolar or fluid product, and the amount that is devoted to the cellular product. One extreme of this series is where the vacuole reaches the maximum, leaving the peripheral or cellular mass at its lowest possible extent; and the other extreme is where the vacuolar product is at its minimum, and the cellular at its maximum. Both of those extremes have an existence in fact; with the latter we shall have nothing to do at present, but the former is simply the perfect transformation of the mammary epithelium into milk, which has been called a deliquescence. Now there is evidently not one law for the function at its height and another law for the function in its subsidence; there is a perfect continuity between the full secretory activity of the gland in the lactation period, and the diminished secretory activity which carries the gland through the involution process to the resting state. The functional stimulus, whatever it is, is simply lowered in the course of involution: it is not that a stimulus of one kind ends and a stimulus of another kind takes its place.

The production of the secretory fluid in the epithelial cell is a process of vacuolation,

The perfect transformation of the mammary epithelium into milk is therefore, in its essence, a process of complete vacuolation. But the importance of this fact is nothing unless the vacuolation process is reduced to its proper place among the great cellular processes of the organism. If the vacuolation process is examined in those cases where its morpho-

or of endogenous cell formation.

On the Ætiology of Cancer, by Dr. Creighton.

logical features are best declared, it will be seen at once that it is the well-known process of endogenous cell formation. The following remarks were introduced into a preliminary notice of the subject appended to the writer's paper, "On the Ætiology of Cancer" in the last volume of these reports.

"The conclusion, then, that we arrive at from the above considerations is that the process of secretion in the epithelial cells of mucous surfaces is essentially a process of endogenous cell-formation. The account usually given of the production of secretion in the epithelial cells is merely pictorial; a passage already quoted [from the manual of Cornil and Ranvier] will serve as an example. 'C'est ainsi que dans les glandes 'de l'estomac on voit des cellules primitivement cylindriques devenir 'sphériques en se gorgeant de sucs, tomber dans la lumière de la glande 'et se detruire en laissant échapper leur contenu.' As so expressed, the life of the secreting cell is nothing else than a chapter of accidents, a succession of events apparently arbitrary in their occurrence. If, however, the law of endogenous cell-formation be applied to this particular form of cellular activity, the various changes in the cell find a rational explanation. The most valid objection to such an explanation will be found to be directed against the terms employed. It is true that in most of the cases that are here referred to the so-called process of endogenous cell-formation, no cells are formed; but that is a paradox which depends on the name having been adapted to only a part of a more widely-spread phenomenon. It may be instructive again to contrast the endogenous mode of cell formation with the mode by division. What distinguishes the former is the collateral production of a vesicle or vacuole containing a fluid, the result of a transformation of the cell protoplasm; in the latter form of cellular activity the cell divides into several pieces, each of which becomes exactly like the original cell. One might say that in the endogenous mode there is a provision for a fluid product, and it is according to many analogies in nature of the adaptation of a general plan to particular ends that such provision may be magnified into the essential feature of the process." (pp. 109–110).

During the subsidence of the function, there is an actual production of cells from the epithelium by the endogenous mode.

The subsequent study of the involutional or subsiding action of the mammary gland appears to fully bear out this theory. In the subsiding process there is an actual formation of waste cells from the epithelium by the endogenous mode, and the weaker the function becomes the more cellular does its product become. Knowing the mode of action in the intermediate terms of what is evidently a continuous series, we are enabled to determine what is essentially the process in the extreme terms of the series. The expression that takes in all the phases of activity in the mamma, from the perfect secretion through the subsiding period to the resting state, is to call the process a process of endogenous cell formation. What may be called the law of the secretion is the law of endogenous cell formation.

Having finished the discussion of this more or less abstract but by no means unimportant point, it will now be convenient to introduce certain additional facts which have been omitted in the description of the involution process. These relate to the same cellular products of the subsiding secretion of which mention has just been made under the name of waste products. They will be frequently mentioned in the subsequent parts of this report: in the physiological part the various normal circumstances under which they are produced and the manner of their safe disposal or utilisation in the organism will be fully set forth; in the pathological part their excessive production, or their production out of due season, or their retention at or near their place of origin will be found to be among the chief factors in the causation of tumours of the breast, and the mode of their production by endogenous cell formation will be found to account for their heteroplastic nature or for the malignancy of the growths which they help to build up.

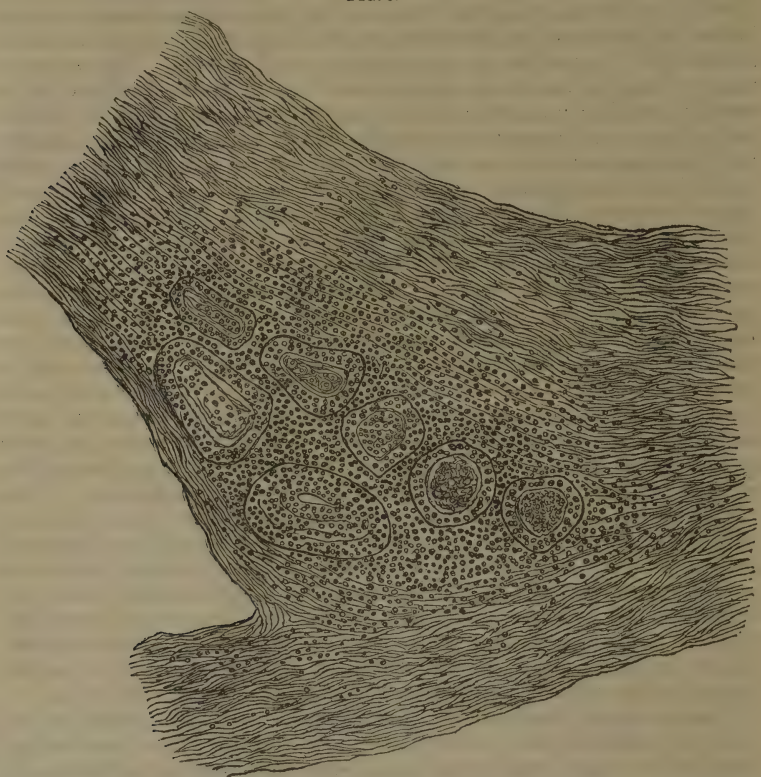
Cellular waste products of the secretion.

App. No. 4.

On the Ætiology of Cancer, by Dr. Creighton.

Fig. 9 represents a section through the corner or angle of a mammary lobule. The preparation was made from a ewe that was killed three weeks after giving birth to a dead lamb and was not milked.

Fig. 9.



From the udder of a ewe that gave birth to a dead lamb and was not milked: the condition three weeks after parturition; a group of seven acini forming the corner or angle of a lobule; many small round cells in the spaces round the acini and in the fibrillar tissue; mucus, mixed with small round cells, in the cavities of the acini. Magnified 150 diameters.

At this period, three weeks after parturition, the udder was still of considerable size, and a clear brownish fluid could be expressed from the teats. The microscopic examination showed in many points a resemblance to the condition of which Fig. 5 is a drawing; there was a corresponding alteration of the epithelium and many acini contained a fluid which coloured purple with the logwood, and was on that account to be taken to be of a mucous nature. But the distinguishing feature of the case was the enormous number of lymphoid cells which were met with both in the acini, in the spaces immediately outside them (known to be lymphatic spaces), and in the interlobular fibrillar tissue.

Cellular waste in the form of small round cells (lymphoid cells).

The section represented in Fig. 9 passes through the extreme pointed end of a lobule, and includes only seven acini; the interlobular fibrillar tissue is for the same reason cut obliquely, and appears thicker than it really is. The fibrillar tissue will be seen to be crowded at certain points with lymphoid cells, often ranged as if in a procession. The spaces round the acini, which in the active secretory state are reduced to a mere line, are here seen to be broad tracts crowded with the same lymphoid cells; it is not unfrequently found in the preparations of this case that the contour of the acinus is completely obscured by the number of small round cells about it. The cells are for the most part round nuclear bodies, but there are found among them the various shapes given

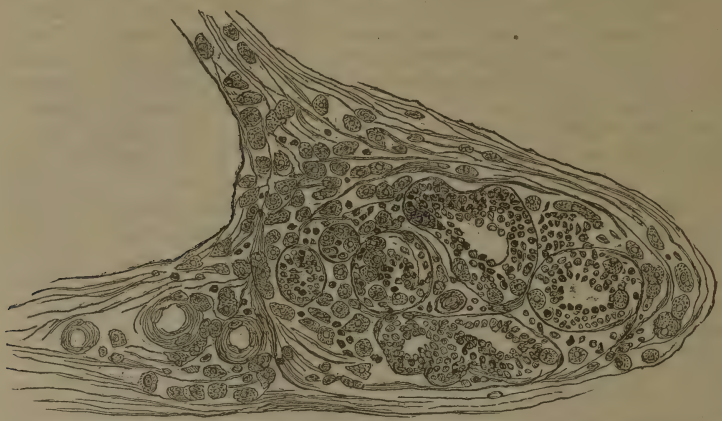
in Fig. 6. On closer examination, it is not difficult to find everywhere traces of the vacuolation or endogenous process within the acini, and it is hardly to be doubted that all of those small round cells are derived from the epithelium by that process. The case is one in which the cellular product of the vacuolation or endogenous process is the predominant, and it will be noticed that the accompanying fluid product is not the fatty fluid of the perfect secretion, but a mucous or albuminoid fluid. The case shows a production of cellular elements from the epithelium which is excessive for that stage of involution, and the fact of the animal never having been milked is no doubt the modifying circumstance; but the same phenomenon is found to occur quite regularly in corresponding stages of the involution process. It will be observed that the greater number of the cells have escaped from the acini into the extra-acinous spaces and the fibrillar tissue, and it is only in those situations that they can be observed in any quantity; but it is probable that the ordinary outlet of the ducts, which are still patent in that stage of involution, must give exit to many of them along with the fluid that is produced at the same time, and which was found in the ducts. Reverting to the case from which Fig. 5 is taken, the same appearance is seen to a more limited extent. There are here and there in the tissue outside the acini considerable heaps of lymphoid cells; and among them are found other and thoroughly well-marked waste products of the involution process, which enable us to place the subject on which we are now entering on a perfectly sound basis of evidence.

The account given provisionally of the completion of the involution process was that the acini, denuded of their perfect mosaic of epithelium, gradually closed upon the nuclear elements that survived from the vacuolation of the latter, and so conducted us to the resting state as figured in Fig. 4. If this were the entire process, we should still have to account for the escape or discharge of a certain quantity of cells from the acini; for the resting cells of an acinus are much fewer in number than those that cover its floor in the middle stage of involution. For example in the case from which Fig. 5 is taken, there are found considerable tracts of acini which have already contracted their circumference to some extent, and there is to be seen at one or two places a lobule which has for some reason or other advanced beyond the others, and reached the extreme contracted state of involution. In such a lobule the cells within the acini are extremely few, from four to six; but what arrests the attention at once in looking at this lobule is the presence in it of a quantity of bright yellow pigment. On closer inspection the pigment is seen to be for the most part scattered about the cells inside the acinus; and if we leave this involuted lobule and search in less advanced parts of the gland, the source of the pigment and the significance of it become clear enough. The other class of waste products which were referred to above as being thoroughly well marked and as affording a sound basis of evidence for the entire question of epithelial waste products, are large granular nucleated cells filled with a bright yellow or golden pigment. The nucleus is often visible; and when it is stained purple with logwood, the cell with its purple nucleus and its bright yellow substance forms to the microscopist a striking and pleasing object. Fig. 10 (p. 138) represents a very common appearance of the large yellow cells. The lobule is in a somewhat contracted state; in several of the acini the pigmented cells which are represented in the woodcut simply as granular, may be seen *in situ*; while a considerable number of them are seen to occupy the interfibrillar spaces outside the acini and the lobule. The latter situation is most characteristic of them. The figure is not taken from a gland known to be in the process of involution; on the other hand it

Cellular waste in the form of large granular pigmented cells.

probably represents an early stage of evolution. But it is inserted here to show once for all the large yellow granular cells to the best

Fig. 10.



Lobule of a mamma near the resting state. Numerous large pigmented cells within the acini and in the interlobular fibrillar tissue; sections of three blood-vessels to the left of the lobule. Magnified 160 diameters.

advantage as regards their size, shape and general appearance, so far as a woodcut can give it.

Out of a great many preparations of the involution process it would be difficult to find one in which the origin and destiny of the pigmented cells together with their place in the involution process was at once apparent. They are not unfrequently seen in the tissue outside a lobule in rows three or four deep; again they are found in the interfascicular spaces among the lymphoid cells that have been already mentioned. Inside an acinus they are found seldom in greater numbers than one or two, but in that position they do not always possess the definite characters that they often show elsewhere. What one sees inside an acinus is, as it were, certain round discs or other irregular forms of pigmented substance generally bestowed round a nucleus; this is a common appearance in the preparation from which Fig. 5 is taken. Finally, as has been already said, the same preparations show in the involuted lobules that they contain, a more or less amorphous appearance of the pigment within the acini, and in sets of preparations from other animals (especially the rabbit), showing the advanced involuted state, the surface of the involuted lobules is found to be

Fig. 11.

A pathological lobule. The uppermost acinus shows the pigmented cells as epithelium *in situ*. Magnified 160 diameters.

strewn with numerous grains of pigment of a brownish colour. Putting together those facts collected from the involution process alone, a theory of the origin of the pigmented cells might be made out. But the question of their origin and significance is greatly simplified by anticipating so far the study of the evolution process and of certain pathological processes. A drawing of one of the latter may here be inserted. Fig. 11 (p. 138) is the section of a pathological lobulus from the dog: the circumstances of its occurrence do not require to be stated here. It is found among lobuli, most of which show the ordinary appearance of the resting mamma; and this particular lobulus, though three or four times the size of its neighbours, has retained its proportions exactly. All the acini of this lobule have a yellowish tint; but the attention is chiefly directed to the half acinus that is uppermost in the figure. In it the cells are intensely yellow and granular, and most of them show a nucleus; they are also for the most part columnar or club-shaped. They occupy the position of the normal mammary epithelium, and the pathological form that they have acquired makes them, if one may so speak, more epithelial than the mammary epithelium usually is. Yet they are evidently ready to be detached from their epithelial situation, and as a matter of fact the same cells, with trifling modifications of form, are to be seen in considerable numbers in the adjoining fibrillar tissue. In the pathological part of the report many other instances will be given of this peculiar transformation of of the epithelium; what is here desired is simply to show the epithelial origin of the pigment cells of the mamma. So conclusive are all the appearances bearing on this question, that it may be stated in the broadest manner that whenever those large yellow granular cells are found in the mamma, they are of epithelial origin.

Evidence that the large pigmented cells are transformed epithelium.

Having so far stated the evidence for the uniform occurrence of the large granular pigmented cells in the course of involution, and having described their more general characters, we come now to consider what is the exact place that is to be assigned to them in the involution process, and by what considerations they can be brought within the operation of the general law of the secretion, that is to say, the law of endogenous cell formation.

Just as the large colostrum-like cells that are figured in Fig. 8 characterise an early stage of involution, and as the more distinctly nuclear products of vacuolation of Figs. 6 and 9, together with the accompanying mucous fluid, characterise the subsequent stages, so the pigmented cells are found to be characteristic of the last state of involution, and the pigment that belongs to them is to be found strewn over the lobules that have reached the resting state. It has up to this point seemed a satisfactory account of the involution process to say that the acini contracted their area and retained within them a certain number of the cellular bodies that remained over from the vacuolation of the epithelium. But the unexpected introduction of a set of pigment-bearing cells is precisely one of those matters of observation wherein the actual course of nature proves more varied than might have been conceived, and whereby we are led to enlarge very considerably our view of the process.

The large pigmented cells belong to the last stage of involution.

In reviewing the process of involution in the mamma, it might appear at first sight as if the entire cycle of changes in the epithelium, that conduct the gland to the resting state, took place in one and the same set of cells. When lactation stops, the acini may be imagined to possess a mosaic of perfect epithelial cells which have not followed their predecessors in transforming their substance into milk, but which are destined to be the elements that the resting cells of the gland are, after a prolonged process, formed out of. But a cursory view of the

facts will at once show that such is not the case. A preparation has been already described, belonging to an early stage of involution, in which many of the acini had a complete set of vacuolated cells lining their wall, and another collection of similar cells lying free in their lumen; and this fact can mean nothing else than that the cells now in the cavity of the acinus had been shed from their epithelial situation, and had been replaced by another set. In like manner the various forms of cells that characterise the various stages of involution must have resulted from a transformation *de novo* of the renewed epithelium, and not from successive changes upon the same cell. Thus, it is difficult to imagine the peculiar pigment transformation of the epithelium to be anything else than the direct and sole change that those peculiar cells undergo. They are evidently products *sui generis;* they are the kind of cells proper to the later stages of involution, and it may be asserted, by way of illustration, that if the functional stimulus of the gland always remained at the same low point as it is in that stage of subsidence, the gland would produce nothing but those cells. The notion then must be set aside, that the particular set of cells that the gland possesses when lactation stops, are the same which become, after various transformations, the resting cells at the end of involution. The epithelium, which had been constantly renewed during lactation, is renewed also many times before the involution is completed, and before the functional activity subsides. In other words, the formative or plastic activity of the gland goes on so long as its functional activity goes on. As the latter gets weaker, the former gets slower, till a point is reached when there is no further renewal of cells within the acinus, and those last produced remain almost as they are. This common point of enfeeblement for both the formative and functional forces of the gland is a theoretical point; while, as a matter of fact, the acini in the resting state are found to contain, as well as round or oval nuclear cells, a certain number of cellular elements that may be distinguished by their form as belonging to earlier stages of involution.

Successive renewals of the epithelium also during involution.

Thus, in concluding the descriptive account of the process of involution in the mamma, we are left with the important physiological fact that the periodical subsidence of the function is accompanied by a considerable production of cellular waste material. In the earlier stages of involution it is thrown off in the form of such cells as are drawn in Fig. 8, and this class of waste products doubtless find their way out of the gland by the ducts. The cells in Fig. 9, along with the various shaped peripheral masses of the vacuoles, may be taken to represent the waste products of a later stage, and it is seen that the lymphatic circulation is at least one mode of their disposal. Lastly, in the latter part of the process, there are produced the very remarkable yellow cells, and these also find their way out of the gland by the lymphatic channels. The complete description of the removal of the cellular waste of the secretion by means of the lymphatic circulation is postponed till the evolution process has been described.

Summary of the waste products of the involution process.

There remain for discussion, in connexion with the process of involution, two points of a theoretical nature. One of these will deal with the considerations by means of which the phenomenon of the large granular pigmented cells can be brought within the law of the secretion, which is held to be the law of endogenous cell-formation; the other point may be briefly disposed of at once.

In the state of active secretion of the mamma, it is convenient to suppose that each epithelial cell that is used up in the formation of the milk has been at one time a perfect polyhedric cell of a homogenous or finely granular protoplasm and with a central nucleus, and that it has rapidly undergone the cycle of changes whereby its whole substance has

been converted into milk. But it is not necessary to suppose that the same should be the case when the function is not at its full force, and is in fact slowly subsiding. The plastic or formative activity of the epithelium must continue, as has been argued, so long as the functional activity has not entirely come to a standstill. But it is not at all probable that the same perfect mosaic of polyhedric epithelium is reproduced at every successive step throughout the whole period of involution as well. For example, if the plastic activity of the gland be viewed for a moment, apart from the functional, and if a point of time be taken, say towards the end of involution, it is not to be supposed that the acini of the gland, at that point of time, would be clothed with a layer of perfect polyhedric epithelium. On the contrary, the nearer is the approach to complete cessation of the gland's activity, the more crude, so to speak, are the successive renewals of the epithelium. The importance of this theoretical statement will appear when the process of evolution is described.

The renewals of the epithelium during involution are not in the form of perfect polyhedric epithelial cells.

The importance of the other theoretical point reserved for consideration will hardly appear till the pathological part of this research is reached; but the proper time for its discussion is now.

As we were led to view the ordinary transformation of the epithelium into milk as a process of extreme vacuolation and to refer it to a place under the law of endogenous cell formation, so we come, at the other end of the scale, to refer the phenomenon of the granular pigmented cells to the same law. The superficial objection to calling the production of milk a process of endogenous cell formation is that there is in it no formation of cells at all. The objection to classing the granular pigmented cells among the same phenomena is that there is in them nothing endogenous or vacuolar. The explanation of those apparent anomalies is furnished by a method of proof that has already been put in force. Directing attention again to the well-defined vacuolation process in the cells, which marks the middle stages of involution, it will be seen that various degrees of vacuolation of a cell occur, and that there is a correlation between the extent of the vacuole and the extent of the associated cellular mass which is generally on the periphery. It often happens that the vacuole is large, occupying almost the whole substance of the cell, and that the solid part of the cell, that part of its substance which gives it an individual existence and a shape, is nothing more than a delicate ring (in profile), with a slight crescentic thickening of coloured substance at one side. It is by observing the varieties of this peripheral coloured element of the vacuolation that the significance of the process becomes clear. Instead of being a thin rib-shaped or crescentic body, it is often of a rhombic or of a hemispherical form, and the latter forms, again, shade off gradually into the round nuclear bodies which are sometimes found lying as if on the ring of the vacuole, but often also found as free cells in its centre. Again, cells are now and then found that have both the crescent-shaped peripheral mass and the free round cell in the vacuole, and this may be considered as the most comprehensive type of vacuolation. Here, then, the process is evidently the process of cell-formation by the endogenous mode; and if the vacuoles of secreting cells were only found to contain several small round cells in their cavity, instead of one, the most rigid and inelastic conception of endogenous cell-formation would be completely satisfied. But the plurality of free round cells in the vacuole, although it is often held to be an essential part of the definition of endogenous cell-formation, seems to be oftener a pathological phenomenon than a physiological. Regarding, then, the epethelial cell which is subjected to this process as containing a fixed quantity of substance, the more of it that is devoted to fluid transformation, the less is the amount of the co-ordinate cellular product. There is

The large pigmented cells are also produced according to the law of endogenous cell formation.

a vanishing point for each of the two factors in the process respectively. The one vanishing point is where everything is fluid, the other vanishing point is where everything is solid; and yet the law of the cell's activity is the same in those extremes as in the intermediate degrees. Both of the vanishing points have an existence in fact. The perfect formation of milk is the one, and the purely solid product of the epithelium is the other; the one coincides with the full force of the functional excitation, the other with its extreme enfeeblement.

There are several matters of observation in connexion with the granular pigmented cells that require to be stated in order to redeem the somewhat theoretical, and, it may still appear, fanciful account of the conclusion of the involution process. In the mamma of a cat that was killed four weeks after the young were taken away, the acini were found considerably reduced in size; they contained, very uniformly, ring-shaped vacuolated cells, but they had everywhere as well a yellowish colour, and the yellow tint did not extend to the other tissues of the gland. On closer examination it seemed that the yellow colour was in the fluid contents of the vacuoles, and there appeared to be traces of the yellow granular cells in the fibrillar tissue outside the acini, in the same position as they are clearly to be seen in other preparations better adapted for the purpose. Unfortunately the appearances in this case were always somewhat indefinite, although several sets of preparations were made from it. But to supplement that defective evidence, it may be stated that in a remarkable case to be mentioned hereafter, there was found distinct vacuolation of the pigmented cells outside the acini, the fluid contents of the vacuole being distinctly yellow. Again, in the case of a cat nine days after the end of lactation, which has been used for illustration several times already, the yellow granular substance within the acini seemed to break up into a number of round disc-like bodies which were remarkably suggestive of red blood corpuscles. It is not desired to follow this subject at present further than to recall the fact that the pigment of the granular cells is not unfrequently seen strewn over the involuted lobules, having quite the look of amorphous masses of hæmoglobin. The resting cells of the acini, or at least some of them, are in all probability the original nuclei of the granular pigmented cells; the latter give up their pigmented cell substance, but their nuclei remain. These facts may point to a lingering secretory activity in the epithelium that is transformed into pigmented cells. But the greater part of the large yellow cells are thrown off from the acini entire and find their way out of the gland entire. Their functional importance is, as it were, so slight, that they are actually thrown off from the gland before the function is performed; and this consideration leads us to speak, in the briefest possible manner, and as a conclusion to the first part of the inquiry, of the significance of the solid or cellular products of the epithelium as regards the function. From the functional point of view, or from the standpoint of usefulness, the fluid product of the epithelium is the only one of the two that is properly speaking a secretory product. But the other or cellular product is all the while potentially present; and it is precisely when the fluid product ceases to be useful or to be required, that the cellular product asserts itself. This cellular product, so far as one can say, does not become itself useful in its turn; it is indeed spoken of as a waste product. But the formation of the useful product cannot come to an end without the temporary formation of a quantity of waste material. The periodical subsidence of its function costs the mamma a good deal of useless cell formation, and we shall have occasion to show immediately that the re-establishment of its function, extending over a longer period of time, costs it a good deal more; while the waste cells produced in both of those processes and in all other enfeebled conditions of the secretion)

The relation of the waste cells to the proper secretory product of the epithelium.

have it in their power to become, and sometimes do become highly dangerous elements of disease.

Section II.—The Evolution of the Mamma.

It has been already explained that the term evolution of the mamma is used to describe the periodical process by which the gland, after each period of functional rest, is step by step rehabilitated with its full structure, in readiness for the next period of suckling. If an animal is killed a day or two before parturition, the mamma is found to possess fully expanded lobules and acini, and the acini to have the mosaic of perfect epithelium. Preparations of the mamma at this period are in fact better fitted to show the perfect form of the epithelium than preparations taken from a gland in the full course of lactation. The beginning of the evolution process must be held to coincide more or less exactly with the beginning of pregnancy. Important changes in the gland are observed at early periods of pregnancy, and the evolution is found to proceed, in its later stages, so exactly hand in hand with the growth of the embryo that it is necessary to suppose the first step towards the preparation of the gland to be contemporaneous with the early changes in the uterus, although, as a matter of observation, little or no alteration of the resting state is found till the embryo is somewhat grown. We thus arrive at the important fact that the evolution process is an exceedingly slow process, in respect of the object to be attained, and that it occupies, generally speaking, the entire period of gestation.

The period at which the evolution of the mamma begins.

The evolution process, as about to be described, has been studied chiefly in the cat. Casual preparations have also been used from the sheep and guineapig, and a large amount of confirmatory evidence has been obtained from a series of cases in the dog, which were made use of under the following circumstances. A series of 16 cases of mammary tumours in the bitch was collected for the purpose of examining the tumours; the tumours for the most part affected only a limited area of the chain of glands on one side. In three of the cases the entire chain of glands was obtained, the animals having been killed in anticipation of a fatal termination of the disease. It was found, on carefully examining the other 13 cases of tumours, which were removed by operation, that no fewer than 12 of them had distinct fringes of mammary tissue round them, which by the side of the tumour, was to be accounted normal. Those 15 cases certainly did not, so far as was known of the history of the animals, exemplify the physiological processes of evolution or of involution. But the microscopic examination of them showed that they were each of them the subject of a certain feeble kind of activity, which often resembled that of the earlier stages of the evolution process, although the excitation to it was not the same. They seemed to show, in fact, that whatever was the stimulus that stirred up the dormant activity of the gland, it commenced in the track of the evolution process, and that it rarely got beyond the earlier stages of that process, but continued to act upon the gland, so long as it lasted, at a uniform low degree of force. As regards the origin of the tumours, sometimes multiple, that occurred in portions of the chain of glands, this feeble activity was of the highest significance, while the cases were at the same time found to illustrate the same effects of weak functional stiumlus as were found in the physiological processes, and to coincide rather with the commencing stimulus of the evolution process than with the subsiding stimulus of involution. The series of cases in the cat on which the account of normal evolution is mainly based were 11 in number; two of these were known to be cases of *primiparæ*. They were fairly representative of the various stages of pregnancy, as estimated by the size of embryo. The newborn kitten may be taken to be

The material used for the study of the evolution process.

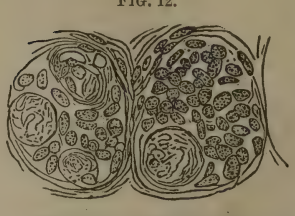
about 5 inches long, measured to the root of the tail. The youngest litter were $1\frac{1}{2}$ inches long, and the intermediate sizes of $2\frac{1}{2}$, 3, $3\frac{1}{2}$, and 4 inches were found, as well as fœtuses almost full grown. There was on the whole a remarkable correspondence throughout the various cases between the size of the fœtus and the stage of evolution of the mamma in the parent. Thus in two sets of fœtuses that were nearly 5 inches long and with the hair grown, the mammæ of the parent showed the most minute resemblance, and they both resembled the condition in the udder of a ewe that was pregnant with a fœtus about 10 to 12 inches long. Again, the mammæ corresponding to the fœtuses 3 to 4 inches long had all an equally characteristic appearance. Greatest diversity occurred in the earlier stages of pregnancy. Thus, in a cat with fœtuses $2\frac{1}{2}$ inches long the mammæ were found in a condition not further removed from the resting state than in a cat with fœtuses of $1\frac{1}{2}$ inches, and considerably less advanced in evolution than in a third cat that had also $2\frac{1}{2}$ inch fœtuses.

The first stage of evolution.

Those three cases taken together represent the earliest appreciable progress towards evolution, and the condition found in them will now be described. In naked eye characters the glands differed little from those in the resting state. Their substance was of no great thickness, tough on section, and with the gland tissue proper separated into islands or bands by tracts of connective tissue, with or without fat; the larger ducts could be seen radiating towards the nipple, and the open mouths of them and of large vessels were conspicuous in cross sections. On microscopic examination the acini had already advanced from the resting state both in size and in other particulars. In point of size they were perhaps half that of the perfect acinus; the infundibular or trefoil-like appearance of three or more acini communicating was much more frequently observed in these preparations than in those of any other condition of the gland, and this circumstance made it difficult sometimes to estimate the size of a single acinus. The cells within the acinus were many of them the same as the round or oval nuclear bodies of the resting state, although more numerous; they occupied the cavity of the acinus generally. But among the nuclear cells were a few of a totally different kind. These are no other than the large yellow granular cells that have been already described as characterising the later stages of involution. Fig. 12 is a drawing of two adjacent accini from the mamma of a cat with fœtuses $2\frac{1}{2}$ inches long; it will be seen that one acinus contains three of those large pigmented cells and the other one. It is to be added, in explanation of the figure, that the large cells have exactly the same yellow colour as the corresponding cells of involution, and that some of them appear to have two or even more nuclei at different parts of their periphery. It is necessary before proceeding further with the account of these earliest products of evolution to repel an objection that may be made. There is no possibility whatever of confounding them with the last products of involution, the existence of which has been already proved. It is true indeed that traces of pigment remain in the gland after the involution process has been completed; but it is either in the form of the entire pigmented cells which are still detained outside the lobule in their passage from the gland, or it is in the form of grains of free pigment scattered over the surface of a lobule, or lying among the resting cells of an acinus. Except under those circumstances the yellow pigment is

The large granular pigmented cells reappear in evolution.

Fig. 12.



A pair of acini from the mamma of a cat pregnant with fœtuses $2\frac{1}{2}$ inches long. The acinus on the left hand contains three large yellow cells, and that on the right contains one. Magnified 500 diameters.

Evidence that the pigmented cells are produced in large numbers in the first stage of evolution.

not present in the gland after involution is completed, and there can be no doubt that the large yellow cells found within the acini in the early stage of evolution are characteristic products of that stage.

In the three cases with small fœtuses grouped together as representing the first stage of evolution, the pigmented cells were found in large numbers, indicating a very considerable cellular productiveness of the acini, and there were certain instructive differences as to the situations in which they were found. In the most advanced of the three, the lobules were considerably expanded, and the acini showed a distinct central space and an arrangement of the cells on the wall; there was in fact an appreciable advance in evolution, and the condition came very near that which will be described as characterising the next definite stage of the process. Now, when the teats of this animal were squeezed, during life, to find out whether the gland contained milk, there issued from the teats not a fluid substance, but a solid friable substance of a yellowish-brown colour in the shape of cylinders or plugs, which broke off in short pieces as they reached the orifice of the nipple. On examining this substance with the microscope, it was found to occur as rounded masses or oblong casts, in neither of which was the form of individual cells easily made out. On proceeding with the dissection and exposing the mammæ *in situ* the ducts were seen radiating from the periphery towards the nipples, as they are often seen where the gland has not its full parenchymatous density, but in the present instance they were obviously filled with a yellow material, the same as was expressed from the nipple. The yellow contents were readily seen in sections of the prepared gland, and they were found to consist of closely-packed masses of the large yellow cells. In the same preparations the yellowish cells were seen to be still within the acini at certain points; they were also found, as they very commonly are, in the interlobular fibrillar tissue.

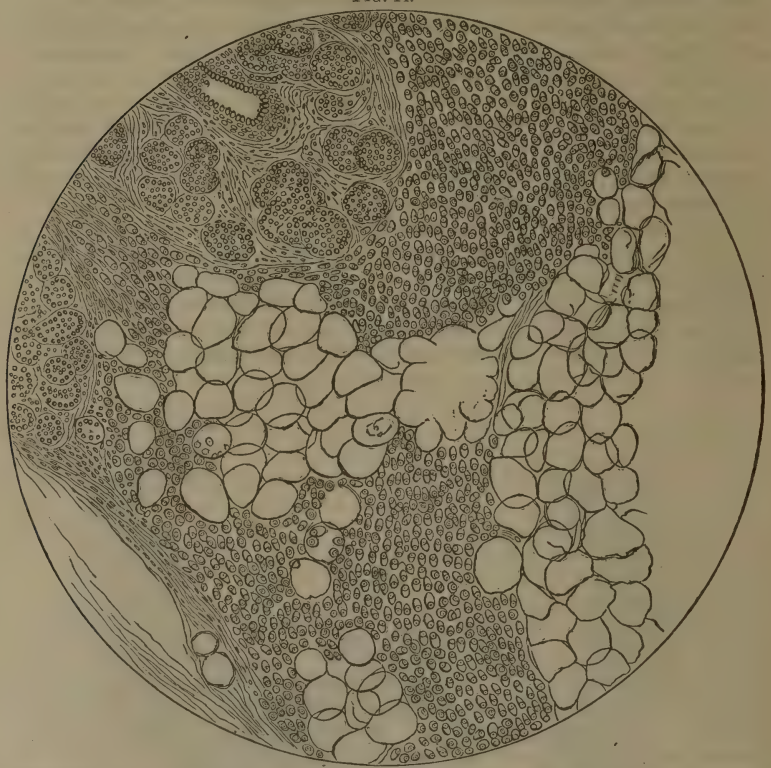
Fig. 13.

From the mamma of a cat pregnant with fœtuses 2½ inches long. Oblique section of a duct, showing collection of large yellow cells in its submucosa, and the same bursting into its lumen. Magnified 150 diameters.

But the strangest position in which they were found was the loose submucous tissue of large ducts. There they occurred closely packed together in one or more rows, and in two or three places where they were collected in the submucosa in largest numbers, was observed the phenomenal appearance of which Fig. 13 is a drawing. A rounded

cluster or knob of the characteristic yellow cells, for the most part with a nucleus visible, is seen to have burst through the epithelium into the lumen of the duct, and to be followed up by several rows of the same cells in the submucosa converging towards the breach in the epithelial wall of the duct through which the others have already passed. There is no doubt that a very large number of the pigmented cells in this case left the gland by way of the ducts, and that they entered the latter, not directly from the acini, which were probably not in open communication with the ducts at the time when the yellow cells were being formed, but by first escaping through the wall of the acinus, then traversing the submucous tissue of the duct, and finally breaking through into the latter at a convenient place. But that is certainly not the only mode of their escape from the gland, and, indeed, it has been observed in the preparations of this one case only. Fig. 14 is from another

Fig. 14.



From the mamma of a cat in an early stage of evolution. The left-hand side of figure shows portions of two lobules, and the rest of the figure shows the fat tissue outside the secreting structure crowded with *the large yellow cells*. Magnified 90 diameters.

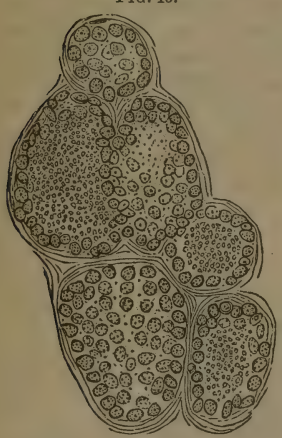
case in the cat, with 2½ inch fœtuses, and though it will have to be referred to again, it is introduced here to show the very considerable numbers in which the large pigmented cells are thrown off in evolution, and the mode of their disposal. The left-hand side of the figure shows portions of two lobules; with a higher power it may be seen that some of the acini contain the large yellow cells in their interior, and, indeed, the two acini of Fig. 12, which contain several yellow cells, are drawn from another part of the same preparation. Between the two lobules, the fibrillar tissue is occupied with a procession of those pigmented cells, along with a number of round and elongated nuclear cells, which are

coloured with the staining fluid throughout and have no pigment around them. The right of the figure shows an enormous collection of large nucleated cells, which are all of the same pigmented kind. They have penetrated into the fat tissue about the gland in the manner that the figure shows. The cells have their nuclei almost uniformly at one end or on one side; several of the largest of them have two nuclei, also excentric, and a few of them are distinctly vacuolated, the vacuole containing a homogeneous fluid substance of the prevailing yellow colour. The case will not be further described until the general question of the disposal of cellular waste by the lymphatic channels is considered in the next section.

The second stage of evolution.

Proceeding to the next well-marked stage of evolution, a certain definite appearance of the gland is found to be common to the cases where the fœtuses were 3 to 4 inches long, and an approximation to it is found in some parts of the gland in the most advanced of the group of three cases representing the first stage. Fig. 15 represents this characteristic appearance. The acini are about two-thirds of their full size, and their arrangement in clusters within the lobule can be seen more clearly than in any other condition of the gland. The cells within them are still of the nuclear kind, that is to say, they have no broad fringe of protoplasm round them; and although there appears to be a definite short interval between each cell, there is not even a narrow fringe of protoplasm to be seen round them. They are, however, distinctly larger than the cells of the resting state, and than many of the same class of nuclear cells in the stage that has just been described. They form a complete covering to the floor of the acinus, being arranged, as has been said, in regular order with definite intervals between them. It can readily be conceived that this orderly arrangement depends on the re-establishment of the regular meshes of the basement membrane, although the latter are not easily made out. A very regular polygonl meshwork of transparent fibres of uniform thickness and without nodes has been seen in the very small acini of one of cases in the tumour series, where the gland was in a condition resembling that of an early stage of evolution. Besides the regular order of the cells in the floor of the acinus, those forming the circuit round it, as seen in the profile view, are also placed in a regular line with short spaces between them.

Fig. 15.



From the mamma of a cat pregnant with fœtuses 3½ inches long. Some of the acini contain a granular material. Magnified 300 diameters.

First appearance of a fluid secretory product.

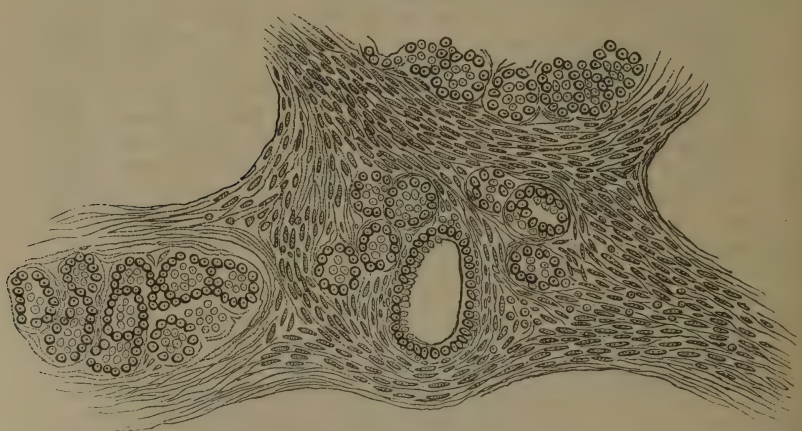
Another distinguishing feature of this stage is the presence in the cavities of the acini of a peculiar granular material, the nature of which has not been found out. In many acini it takes on the colour of the staining fluid to a certain extent, in others it retains its greyish-black appearance, while in others it is found to be mixed with or to pass gradually into a fluid substance the vesicles of which have a peculiar glassy appearance.

In the glands now considered corresponding to 3 to 4 inches length of fœtus, the evolution has advanced to a point when there is no further trace of the large pigmented cells, whether in the acini or in the interlobular fibrillar tissue. In the former group of three cases, showing the early evolution changes, there was one that came nearest to the later

stage of evolution, which is at present under consideration; and in that case the pigmented cells were already collected in large numbers in the ducts, and were seldom met with at or near the place of their origin. The season of their production from the acini had already passed. But in the two other cases of the same group, which were known from other circumstances to be at an earlier stage, the pigmented cells within the acini were comparatively numerous. But although the later stage of evolution is not characterised by the presence of large pigmented cells in the tissues of the gland, it is characterised by the presence of no less important cells of another kind that are also to be seen in transit along the interfascicluar spaces. The absence of pigment in these cells makes it exceedingly difficult to prove their identity : that is, to prove where they come from and where go to. But if the whole of the following considerations are duly weighed, what is here contended for will probably appear a reasonable contention. If reference is made to Fig. 12, representing a pair of acini in the first stage of involution, there will be seen, in the notch between the upper part of the acini, a small number of spindle-shaped cells lying in the interacinous tissue. If, again, reference is made to Fig. 14, from the same case, the pigmented cells in the fibrillar tissue between the lobules will be seen, or rather, can be seen with a higher power, to be mixed with a number of round and spindle-shaped cells of a nuclear kind, and to be themselves drawn out into elongated or spindle form. In the tissue surrounding the lower of the two lobules, these nuclear non-pigmented cells are in great abundance. Finally, Fig. 16, a careful drawing of the condition of the mamma in evolution

The characteristic waste cells of the second stage.

Fig. 16.



From the mamma of a cat pregnant with fœtuses 3 inches long. At the upper border, the outermost row of acini of a lobule; on the left, below, a small lobule; at the two sides, curves corresponding to the boundaries of two other lobules; in the centre, a duct with a group of acini round it; *the interlobular tissue crowded with spindle cells.* Magnified 160 diameters.

corresponding to a 3-inch fœtus, shows the tracts of interlobular fibrillar tissue, as well as the thinner bands of fibres between acini, to be crowded with spindle cells. Now it has already been contended, without any hesitation, that the many small round cells, which are seen to occupy the interlobular tissue in Fig. 9, representing a stage of involution, are waste products of the epithelium ; and if all the cells that one had to deal with in this respect were either large pigmented cells or small round nuclear cells, there would probably be no great difficulty in obtaining credence for the statements that are made. But spindle cells have always been considered the especial weapons of the connective-

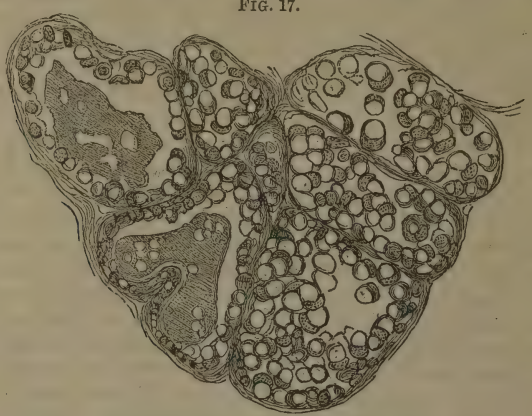
tissue theorists, and one cannot but feel the hazardous nature of an attempt to prove that spindle cells may have some other than a connective-tissue origin. As Professor Rindfleisch says: "Here, if anywhere, the teaching of Virchow remains uncontroverted." Professor Virchow is also the author of an excellent witicism which may well deter anyone from trying to extend further the province of the wandering cell. The present century, he remarks, is the *Wanderjahrhundert*, and everyone feels a natural reluctance to throw himself into a movement which is thus ingeniously made to appear as if it were a passing fashion. The reactionary tide might seem in this case to be the tide that leads on to the sounder conclusion. But with every desire to keep the theory of wandering cells within due bounds, and without ignoring the deeply-rooted opinions as to the origin of all spindle cells, it has appeared necessary, in view of the facts of the case, to assert that the spindle-cells of Fig. 16 are also waste products of the epithelium, and that their spindle form is due chiefly to the pressure that they suffer in passing along the interfascicular spaces. This assertion is founded on a large body of evidence, some of which can be more conveniently stated in the third section of this report, which deals with the disposal of the epithelial waste products in general. It remains to be said, in this place, that the crowding of the interlobular tissue with spindle cells can be observed throughout the early and middle stages of evolution, in all the cases that exemplify those stages. In the early stages they are often found among the pigmented cells in the fibrillar tissue, which may be themselves elongated and spindle-shaped, and there is little doubt that many of them are simply the nuclei of the latter, which have lost their investment of pigmented substance. In the later stage of evolution, a gland that has the interlobular tissue full of spindle cells, as in Fig. 16, may show not a single trace of pigmentation, and the spindle cells must be supposed to be only slight modifications in form of the special kind of waste products that characterise the stage of evolution subsequent to the period of pigmented-cell production. The impression that the spindle cells in the fibrillar tissue are elements that have been conveyed thither, and have not resulted from the proliferation of the fixed connective tissue elements of the part, depends on various appearances. There is, in the first place, a peculiar orderly arrangement of the cells as if they were in a procession, following the direction of the interfascicular spaces with their long axis. Again, they visibly lie in many cases in a comparatively wide space between two fibrils. Lastly, they are crowded upon one another at some points much more than at others, and in those situations where they are most numerous, there is nowhere a single trace of the division of nuclei or any other evidence that a process of multiplication of cells is going forward. In contrast with the condition of the fibrillar tissue in those states of the gland, large tracts of it may be carefully examined in other states, such as a resting condition that has lasted some time or the atrophic condition of old age where it is very abundant, without finding in it almost a single cell of the kind here spoken of. Even if it were seriously argued that those spindle cells are the connective tissue corpuscles, an adequate motive for their excessive production could not be found. Some sort of random theory might no doubt be built up, as for example, the following: In evolution of the gland, the connective tissue between the lobules has to be got rid of. To this end, there is a return of the fibrillar connective tissue to its original cellular state. When the fibrillar tissue is reconverted into the spindle cells from which it came, the latter being transportable are conveyed away, and in this manner the amount of interlobular tissue is reduced to the desired minimum.

Whether that is so, is entirely a question of fact, and whether any other alternative theory that the imagination might be trusted to construct, is true, becomes also a question of evidence; and the entire question of the origin and disposal of the spindle cells may be left with the evidence which has been given and with that to be added in the next section.

Completion of the evolution process.

We come now to the late stage of evolution, immediately preceding the actual formation of milk. Fig. 17, is a drawing which might have been made from any part of the mammæ of two cats which were each pregnant with fœtuses almost full grown and covered with hair. The same appearance might also have been sketched from many parts of the udder of a ewe that was pregnant with a fœtus about a foot long. At the stage of evolution, the description of which we have now reached, the glands are voluminous, and of the almost uniform parenchymatous consistence of the fully-developed state. In the case of the ewe just mentioned, a clear brownish fluid could be expressed from the teats. On microscopic examination, the lobules are fully expanded, and the interlobular tissue forms quite thin septa. The entire field of the microscope is occupied by the closely-packed acini, which are of the full size. The appearance that is characteristic of this stage is given in Fig. 17. Many acini are filled with a mucous fluid, colouring with the

Fig. 17.



From the mamma of a cat pregnant with fœtuses almost full grown. Vacuolation of the epithelium; two acini on the left containing mucus. Magnified 300 diameters.

Production of mucus from the epithelium precedes the secretion of milk.

staining agent, and apparently penetrated with a large number of round vesicles. The floor of the acinus, and the circumference of it when seen in profile, are occupied by a complete set of cells in regular order, all of which are vacuolated, and most of them in exactly the same manner. If the figure is referred to, it will be seen that the peripheral mass of the vacuolated cell is almost always large; it has a somewhat oblong or reniform shape, and shows a nucleolus. Looking at the floor of an acinus, an impression is got which it has been found difficult to convey in the drawing. The excentric nuclear bodies all look not so much as if they were situated on the periphery of a round vacuole, as that they lay each on one side of the polygonal meshes of the basement membrane. This simply re-opens the former question of the relation between the polyhedric form or outline of the cell, and the regular polygonal space in the basement membrane in which it is set. But if the profile view of the epithelium is looked at, it becomes clear that we have to deal with the same vacuolation as elsewhere; and the peculiar appearance of the floor of the acinus must be owing to the prominence of the fibres of the base-

ment membrane, side by side with the delicate vacuolar outlines. The mucous fluid in the cavities of the acini is obviously the vacuolar product of the epithelium, and it is interesting to note that the period at which mucus was found in the acini in the course of involution, corresponded to exactly the same degree of vacuolation of the cells. It is the period of involution that is represented in Figs. 5, 6 and 9, the two former being from a cat nine days after the end of lactation, and the latter from a sheep killed three weeks after parturition, without having been milked.

It is a somewhat remarkable circumstance that the case of the ewe with a fœtus about a foot long, and therefore far advanced in pregnancy, shows in some places exactly the same enormous collection of small round cells about the acini as in the case of the ewe in the involution process from which Fig. 9 is taken. In both cases they are, in isolated portions of the gland, so numerous as to completely obscure the outlines of the acini. There is no doubt something unusual in the circumstances of each case; but they none the less illustrate the physiological law of their respective processes, and the remarkable parallelism between the same. In the two cases of advanced evolution in the cat, as represented by Fig. 17, there is little or no appearance of cellular waste products outside the acini, and within the acini it is only the fluid waste that is to be seen. Whether the cellular masses that occupy the periphery of the vacuoles in this stage are ever disengaged and thrown off as cellular waste, or whether the cell as now seen is only partially vacuolated but destined to be entirely so, is not easy to decide. It is certain that there are found side by side with those signet-ring like cells, a few in which are nothing but delicate ring-like forms, without any cellular enlargement on their periphery. Again the vesiculated appearance of the mucus in the acini suggests that it is an aggregate of cells entirely transformed into that fluid. Finally, if there is any cellular waste at this stage of evolution, it would be discharged partly by the ducts, along with the mucous or fluid products of the epithelium.

There is but a single step from the period of evolution just described to the perfect state of the epithelial cells which is found a day or two before parturition. The appearance of a mosaic of polyhedrie cells with a central nucleus may be seen in occasional acini of the previous stage, but the protoplasm of the cell is perfectly homogeneous and not at all granular: the nucleus seems rather to lie in the centre of an empty polygonal space. About the time of parturition the epithelium has acquired its granular appearance, and shortly after the birth of the offspring the milk begins suddenly to be formed in great abundance. The milk of the first few days contains a large number of the well-known colostrum cells, which are the last of the long series of imperfect secretory products that have been thrown off all through the evolution process. The appearance of well-defined colostrum cells is very much the same as that of the cells in Fig. 8, which are found within the acini in the earliest stage of the involution of the gland.

The colostrum corpuscles are the last of the series of waste cells of evolution.

The method followed in the account of the involution process, of giving a description of the gland at various well-marked stages of its progress, without any running commentary as to the physiological significance of the same, has been mainly followed also in the account of the evolution; and if it be added that the well-marked stages that have been chosen for description are of necessity somewhat conventionally divided from each other, the preceding account of evolution may be taken as a fairly complete statement of the facts of the case. It now remains, as in the section on involution, to consider by way of summary, what is the physiological law of the gland's activity during the rehabilitation of its structure.

The significance of the cellular processes in evolution.

It has been explained, in the first section, that it took several weeks for the secretory activity of the mamma to run down or to subside, that the gradual subsidence was accompanied with the production from the epithelium of a good deal of cellular waste, and that the conclusion of the process of involution left the gland with all the parts of its framework entire, but with the acini greatly contracted and containing only a heap of nuclear cells. The renewal of the gland's activity begins, roughly speaking, with the commencement of the next pregnancy, and it brings with it, step by step, the rehabilitation of the full epithelial structure which had been lost during the previous subsidence. This rehabilitation is in most animals a very slow process; one may say that it is unnecessarily slow, in respect of the object to be attained. But, as a matter of fact, it is not completed till the term of gestation is at an end. The evolution of the gland is, as it were, distributed over the entire period of pregnancy. Starting then with the resting state of the gland, we are met with the problem, How do the nuclear cells that are left occupying the acini at the end of involution assume the character of nucleated polyhedric epithelium, and according to what law of cellular activity does this rehabilitation take place? If the law of endogenous cell formation is observed during the subsidence of the function, in what way is it observed during its re-establishment? Now, as was contended *mutatis mutandis* in the analogous case of involution, it is not to be supposed that the particular set of nuclear cells with which an acinus is furnished when evolution begins are the same that, after various transformations, spread over a very long period, become the polyhedric epithelium of the secretory stage. On the contrary, there is no more certain fact in the study of the mammary evolution than the large production from the acini of various kinds of waste cells at various stages of the process. Fortunately this statement does not depend on any logical putting together of disjointed appearances; the Figs. 14 and 16 are well adapted to show large collections of cells that have been thrown off from the gland. Now, it is in the successive renewals of the cells within the acini, which this fact involves, that we find the successive steps towards perfect epithelium. Each new generation of cells is more like the polyhedric nucleated epithelium than the preceding. We know no process of simple multiplication of cells by which the nuclear elements of the resting state could produce polyhedric epithelium, even if the process were continued through many generations. If they multiplied, as no doubt they do, they would produce nuclear cells like themselves; and if we were tied down, in our explanation, to a mere process of proliferation or a formative process, it would be impossible to understand how those nuclear cells ever came to have such descendants as the perfect epithelial cells. But we have already seen that the activity of the mamma is always double; there is both a formative action and a functional action, and those two, in health, always go hand in hand. Consequently, when the re-awakening forces of the mamma are directed to the cells within the acini, the latter not only multiply, but they are at the same time transformed in the direction of the secretion. It is the transforming force and the increasing intensity of the same which is the factor wanting to explain how the nuclear cells at one end of the scale are the progenitors of elements so unlike themselves as the perfect epithelial cells at the other end. This transforming force, as has been said already, does not all at once change the nucleus into an epithelial cell; and another mode of expressing the same fact is to say that the functional excitation is at first feeble. The earliest change noticeable in evolution is the presence within the acini of the large yellow granular cells. Those cells were the last products of the declining secretory force in

involution; they are the first products of its re-awakening in evolution, and it will be shown in the pathological part of the research, that the same transformation of the epithelium is the characteristic effect of any feeble stimulus whatever, applied to a gland in the resting state.

The first step then in the evolution of the gland is the transformation of nuclear cells of the resting state into large granular cells containing yellow pigment. Just as we saw that some at least of the resting cells of the acini were derived from the large yellow granular cells of involution by the latter losing their pigmented granular cell substance and leaving their nuclei behind them, so it now appears that the same nuclear resting cells recommence the cycle of change by acquiring a granular and pigmented investment. In some such way, at least, must one construe the re-appearance within the acini of the large pigmented cell in the early stage of evolution. The change from a nuclear to a larger granular condition is observed elsewhere in the body; Virchow in particular has remarked on the radical importance of this change. Combating the mistake which, as he says, is commonly made of treating white blood corpuscles, lymph corpuscles, and the cells of the follicular tissue of lymphatic glands as if there were no morphological differences between them, and as if they were convertible terms, he points out that there is a distinct act of transformation before one of these can become the other, and that this transformation is no less real than the passage of a cell of the *rete mucosum* to become an epidermic cell. For example, the commonest kind of cell in the parenchyma or follicular tissue of a lymphatic gland is a "naked" nucleus, without a cell body. The latter, he remarks, is of a fragile nature, and may easily be pressed or dissolved away in the course of preparation. By careful handling, the nucleus may be seem to be enveloped in a cell body, but the latter is often so small that it forms merely a slender fringe round the nucleus. The nucleus, although small, then appears relatively large. The cells of the lymph, on the other hand, have a more voluminous cell body, which is also so much more dense that the nuclei become less distinct. Still more is this the case with the colourless blood corpuscles, whose dense and exceedingly granular bodies quite conceal their multiple nuclei, so that the latter are made visible only by reagents or the imbibition of water. Cells with those characters are found in the follicular tissue of lymphatic glands when these are subject to any irritation, and Virchow remarks that among the appearances of this kind are some that speak for endogenous new formation.*

From a morphological point of view, the change from the nuclear resting cell of the mammary acini to the large granular cell of the first stage of evolution is no doubt of the same kind. The increase in size, is however very much greater, and the granular cell body is filled with yellow pigment. The pigmented cells are thrown off from the acini in large numbers, and in the case from which Fig. 14 is taken a large collection of them has been accidentally formed in the neighbourhood of the gland. If this collection is examined with a higher power, it will be found that some of the cells have two nuclei, that the nuclei are all excentric and therefore clearly to be seen, and that a cell here and there has undergone the typical vacuolation, the fluid in its vacuole being of the same yellow colour as the granular cell substance of the others. The pigmentation does not continue into the later stages of evolution, just as it did not commence till towards the end of involution. As the functional stimulus gets gradually stronger, the cells produced within the acini, whatever they may have been when first produced,

* *Cellular-Pathologie*, 4th edition, pp. 210–212.

are thrown off as somewhat large nuclear bodies of a granular appearance, which often acquire an elongated or spindle form in their passage through the interfascicular spaces. The difference between them and the pigmented class of products, is that they have undergone a certain amount of functional transformation within the acini, as evidenced by the presence of a sometimes granular and sometimes fluid material in the acinous cavities; whereas the large granular pigmented cells are thrown off unchanged. It may be recalled to mind once more that the pigmented cells do show a tendency to become vacuolated, and otherwise to lose their cell substance after they have left their proper functional habitat. Coming to the last stages of evolution, we again reach familiar ground. In the glands corresponding to almost the full size of the fœtus, there is perfectly typical vacuolation of the epithelium going on, with the formation of mucus as the fluid product; and this vacuolation takes place in cells that have now recovered the polyhedric form of epithelium. By this time the secretory excitation of the gland has increased so much in intensity that the functional transformation is only slightly different from that of the perfect state. Those slight differences are however instructive. They enable us to interpret aright the nature of the secretory process when the function is at its height, and when the transformation of the epithelium has no morphological features; and they equally help to clear up the obscurities of the process in its earliest stage. The parallelism with the involution process is complete. We again find ourselves in a progressive series of vacuolation changes, with a correlation between the fluid and cellular elements of the vacuolation. At one end of the series, everything is vacuole, and there is no cellular production; at the other end of the series everything is solid or cellular, and there is no vacuole. In conclusion, then, the glandular activity in its re-establishment, no less than in its subsidence, follows the law of endogenous cell formation, and that is also the law of its action when it is in its full career. Again, the evolution is accompanied by much cellular waste; and the cellular waste of the evolution is more than that of the involution, in proportion as the former process is spread over a greater space of time.

Parallelism between the involution and evolution processes.

Section III.—The Disposal of the Cellular Waste in the Processes of Involution and Evolution of the Mamma.

The main physiological facts of the two preceding sections may be said to be the performance of the mammary function according to the law of endogenous cell formation, and the production, during involution and evolution, of a large amount of cellular waste, arising from the operation of that law in the subsiding or immature periods of the function. The present section will be devoted to a consideration of the further progress and ultimate disposal of the waste cells.

Summary of the various kinds of waste cells of the secretion.

It is necessary, at the outset, to recapitulate the various forms of cells thrown off at different periods. They may be classed in three groups, subject always to the reservation that there is a gradual transition between them. The first kind of waste products are the familiar colostrum cells, which approach most nearly, whether at the beginning of involution or the end of evolution, to the perfect secreting cell. The second kind are the more or less nuclear bodies of somewhat various shapes, which are the survivals of well-marked vacuolation of the epithelium and are usually associated with a mucous fluid; they characterise the middle period of both processes. The third kind are the very remarkable large pigmented cells, which are the latest products in involution and the earliest in evolution. The disposal of one half of the first of

those varieties is a matter of common observation. They are got rid of by the ordinary outlets of the secretion viz., the ducts, and they are found mixed with the first milk in large numbers. The corresponding imperfect products at the close of lactation are no doubt disposed of in the same way, although the strong flow of the secretion is in this case wanting to bear them before it. The ducts are, however, found for several days after lactation, and even as late as the second week, to be filled with a thick milky substance, and it is not uncommon for a fluid to escape from the breasts for some considerable time after weaning. The two other kinds of waste products are got rid of usually in a different way. Preparations have already been described and figured which show them to be collected about the acini and in the fibrillar tissue. The acini, at the periods when those cells are produced, do not appear to communicate freely with the ducts; the cells therefore find their way into the lymphatic channels of the gland, whence they are conveyed away. Those two kinds of cells, though they differ much in size and in other respects, may be classed together for the present purpose. But as might be surmised, it is the pigmented cells that are again the infallible sources of observation, and they will be made to sustain the proof of the statements that apply to both kinds alike. They are perhaps not the most abundant of the waste cells, but their unmistakeable yellow colour makes them by far the most valuable for demonstration, and enables the whole question of the disposal of the cellular waste to be treated much more objectively and briefly than it could otherwise be.

The disposal of the cellular waste is best studied in the case of the pigmented cells.

Now, as regards the large yellow granular cells, they are most commonly found outside the acini in the position given in Fig. 10 on page 138. Having once entered the lymphatic spaces they continue their progress in the same. But a case has already been described and figured which constitutes a remarkable exception to the general rule. In it the yellow cells are also found to have left the acini, but they travel along the submucous tissue of the ducts, and at convenient points break through into the latter, which were found throughout the gland to be filled with them. Apart from this case, there is the clearest evidence collected from a large number of preparations, that they are conveyed directly from the mamma to the lymphatic glands which are situate at each end of the mammary chain. Those at the upper end are the axillary glands; those at the other end are the special and chief lymphatic glands of the mamma, and they demand a separate description.

The waste cells are conveyed to lymphatic glands.

It has been already mentioned that the inguinal portions of the mamma rest on cushions of fat, which are sometimes of great thickness. Thus, in two cases of advanced involution, in the dog and cat, the lower end of the mammary chain forming a thin layer of tough substance rested on a cushion of fat about three-fourths of an inch thick. In each of the cases there were found in the centre of the fat one or two quite small masses of tissue which proved on examination to be lymphatic glands. In most of the other cases the lymphatic glands have been found of larger size, and placed close to the under surface of the mamma and towards its outer border, where also the fat extends. Sometimes a chain of them is found extending beneath the mamma for two inches or more forwards along the abdominal wall, and these also are always embedded in a certain quantity of fat. They are for the most part long, narrow, and flattened cylindrical bodies, with a hilus extending along the whole length of one edge. The appearance of a hilus is produced by the apposition of two rounded borders, as if the gland had originally been a flat disc-like body like the spleen, and had got folded upon itself. Along the hilus border there are always found an artery and a vein of relatively large size.

Special lymphatic glands beneath the mamma.

Description of the lymphatic glands in a particular case.

From their position, those lymphatic glands seemed to belong to the mamma in some especial way. They were found to vary much in size in the different cases, but it has not been possible to make out that they vary in any exact measure with the periodical changes in the mamma itself. However their relation to the mamma is put beyond all question even by a cursory inspection. One particular case out of a large number is superior to the rest for purposes of demonstration, and it will be briefly described. It occurred in a bitch which had a large tumour occupying a certain limited portion of the mammary chain on one side of the abdomen. The animal was killed, owing to the incurable nature of the disease (secondary tumours in the liver and lung), and the whole chain of glands on both sides was dissected off. The new growth was perfectly circumscribed; and the entire mamma on one side and the greater portion of it on the other were found to have the usual tough fibrous appearance of the gland at or about the resting state, although with an unusual amount of yellowish-brown pigmentation. The attention is specially directed to the inguinal portion of the gland on one side. It had the appearance, as has been said, of a tolerably normal mamma at or near the resting state; it was about a line in thickness and lay upon a cushion of fat half an inch thick. In the midst of this fat and at a distance of about one-quarter of an inch or more beneath the gland, there were found two quite small parenchymatous bodies of a uniform rich yellowish-brown colour, and which proved, on microscopic examination, to be lymphatic glands. One of them appeared as the cross section of a slightly curved disc-shaped mass, and close to its concave surface there appeared the cut ends of two large vessels. The other was a somewhat pear-shaped body placed in the fat in an oblique position.

The microscopic examination, as has been said, showed them to be lymphatic glands. But they did not contain the relative proportions of the various tissues that are ordinarily met with in lymphatic glands. The follicular tissue corresponded chiefly to the thick end of the pear-shaped mass and to the convex surface of the crescentic; the cells of that tissue were of the ordinary lymphoid kind. The surface of the follicles was very commonly strewn with grains of brown pigment; otherwise the follicular tissue was not pigmented. Probably the greater part of the gland consisted of the wide lymph-sinuses and the dense fibrillar tissue of the hilus, through which the former penetrated. The large lymph-sinuses were everywhere filled with the yellow granular cells that have been so often referred to in the first and second sections. Fig. 20, on page 43, is a drawing of a portion of one of these preparations; the enormous preponderance of the stroma of the hilus and of the lymph-sinuses, and the quite rudimentary condition of the follicular tissue will be at once apparent, but the further description of the preparation is reserved for a later stage. The yellow cells are represented in the woodcut simply as granular.

Evidence that the waste cells are conveyed to the lymphatic glands.

It has been already mentioned that the mamma of this case was to the naked eye more pigmented than usual; and on microscopic examination many yellow or brown granular cells were found in and around the acini, which were for the most part only a little larger than in the involuted state. A series of sections was made which included in one piece the mamma, the fat beneath it, and the lymphatic gland in the midst of the latter; and it was possible, in one and the same preparation, to identify in the clearest manner the pigmented cells of the mammary acini with those in the lymph sinuses of the lymphatic gland. Certain tracts of tissue were found running through the fat between the mamma and the lymphatic gland, which were, no doubt, collapsed

lymphatic vessels. None of the pigmented cells were found at any point between the mamma and the lymphatic gland, and that circumstance will now be explained by reference to a preparation from another case. It is the case that has been referred to several times already, and from which the figure on page 146 has been drawn. It represents the early stage of involution in the mamma of the cat, the fœtuses having been $2\frac{1}{2}$ inches long. The acini and surrounding tissue contained numerous large pigmented cells, and so also did the lymphatic glands of this case, a drawing from which latter is introduced afterwards. But the remarkable feature of the case is the collection of the same yellow cells in the fat tissue outside the mamma. It seemed at first sight as if this were a case of the pigmented cells passing through the fat to the lymphatic gland. But a second examination showed that such was not the case. In the inguinal mamma of this case, as in one or two others, there was in addition to the fat beneath the mamma, a small quantity of fat on its upper surface. Fat on the upper surface is unusual; for the mamma, or its loose fibrous investment, nearly always adheres closely to the skin above. Now, on a second examination of the preparations, it proved to be this external layer of fat, and not the cushion beneath the gland, that contained the large collection of yellow cells. It is not at all a fanciful account of the matter to say that the pigmented waste cells had made their escape from the mamma on the wrong side of that organ; they had travelled along channels that were no doubt patent to them, but which led into a layer of fat from which there was no exit. The unusual layer of fat on the upper surface of the gland played the part of a trap to a certain number of waste cells; if they had travelled like the others into the fat on the lower surface, they would have been conveyed to their proper reservoir, the lymphatic gland. The collection of waste cells in the fat in this case is of that exceptional kind that proves the rule; if there had been no obstacle to their transit they would have passed so quickly through the lymphatic channels that the preparations of the animal killed at a particular moment of time would, probably, not have shown a single cell in its passage. The same difficulty of finding cells in some particular act of their life constantly occurs in the histology of the dead tissues. It has been observed, however, in one or two cases that the fat tissue close to the lymphatic gland contained rows or groups of cells, chiefly of the nuclear kind.

With the last-mentioned fact we return to the more detailed consideration of the progress of waste cells that have reached the lymphatic gland from the mamma. So far as the facts have been already stated, the lymphatic glands under the mamma are to be viewed as special appendages of the secreting organ; whatever other function they may have, they are obviously there to receive the cellular waste products of the secreting gland to which they are attached. In the case described, where the lymphatic gland consisted to a great extent of lymph sinuses filled with the pigmented cells from the mamma, it was impossible to resist the notion that the collection of the cellular waste of the secretion and the disposal of the same was its *raison d'être*. Whether all the lymphatic glands in the body participate in this function for the tissues, secreting and other, with which they are connected respectively, is a question that can only be answered by going through the different sets of lymphatic glands one by one; and the yellow or brown pigmentation that has been observed, for instance, in the mesenteric glands of some animals, may in their case also afford a clue. The material of this research has furnished some evidence on the point for one other set of lymphatic glands besides those of the

The function of the special lymphatic glands is to receive the cellular waste of the secreting gland.

mamma. In the case of a cat that proved to have just completed the involution process, there were the usual evidences of pigmentation in the mammæ. The lymphatic glands beneath the inguinal mamma were all streaked on the surface with several yellow lines, just as the mesenteric glands at a certain stage of digestion are streaked with white lines owing to the presence of chyle in their afferent vessels. The axillary glands were streaked in the same way. The presence of pigment in both the special mammary glands and in the axillary glands was easily explained by reference to the state of the mamma. But it was found, on examining the animal further, that there was a chain of lumber lymphatic glands lying along the lower end of the aorta which were streaked on the surface in exactly the same manner. This was at first inexplicable, and threatened to destroy altogether the theory of a special relation between the mamma and the lymphatic glands near it. But an explanation was forthcoming on continuing the dissection. On cutting open the uterus, which contained no embryos but was somewhat larger than in the non-pregnant state, the mucous membrane over a small area in both its horns, about half an inch from the cervix on each side, was seen to have a yellowish colour. On making a transverse cut at those points, a distinct deposit of a yellow substance was seen in the sub-mucosa, and the microscope showed this to be a collection of yellowish-brown pigment grains strewn among the sub-mucous tissue, but not associated with any cell forms. Here then was an organ, known to be associated with the lumbar lymphatic glands, which contained traces of pigment formation in its tissue and which had probably been the source at an earlier period of the very much larger amount of pigment represented by the pigmented cells in the afferent lymphatics and sinuses of the lumbar glands. The production of yellow pigment cells during the involution of the uterus is not mentioned in writings on that subject, so far as has been observed. It would not be an unlikely circumstance if an organ so closely related to the mamma as the uterus is, should be found to be in the course of its involution also subject to the same transformation of its epithelium.

In the above case the pigment cells evidently entered the lymphatic gland by the afferent vessels, from which they travelled into the lymph sinuses of the cortex; and the same order of progress is constantly observed in the other cases. In the lymph sinus of the cortex, at a particular part of the gland, one or two rows of the pigmented cells are found arranged in regular order. Their futher progress, and the changes that await them, have now to be followed up. This part of the investigation will be found to deal with *the general plan of structure and with the function of lymphatic glands.*

Resumé as to the structure of lymphatic glands.

The minute structure of lymphatic glands has been studied by so many observers during the past fifteen or twenty years that there is little room to add anything to the histological details. But there need be less hesitation about offering a re-interpretation of certain of those appearances; and, above all, the whole question of the function of lymphatic glands is open to elucidation, even of an elementary kind. As regards the structure, the lymphatic glands are admitted to consist of three kinds of tissue, which may be seen in Fig 19. The first and most abundant is the follicular, which includes both the round or pear-shaped follicles proper, occupying the cortex of the gland, and the cylindrical continuations of the same which occupy the medullary part of the gland. The follicular tissue consists of dense masses of small lymphoid cells, which lie in the meshes of a fine network that can be made visible by shaking the cells out of it. There is no difference whatever between the cortical follicles and the medullary cylinders as

regards minute structure. The second class of structures are the lymph sinuses. They accompany the follicular tissue throughout the entire gland, forming somewhat narrow spaces around the follicles at the cortex, but widening towards the medulla into spaces round the cylinders of lymphoid cells, which are often as broad as the cylinders themselves. The lymph sinuses are not perfectly open and empty spaces. On the contrary, they are crossed in all directions by a network of bands or fibres, and they are always found more or less filled by cells. But if they are compared with the follicular tissue in this respect, the branching fibres within them do not form anything like so close a reticulum, nor are the cells that lie among the fibres so numerous or so densely packed. The lymph sinuses, even when filled with cells, have a much lighter appearance than the follicles or cylinders, and they are aptly spoken of by Recklinghausen* as the "*lichtere Stellen.*" The same writer also points out that the cells in the lymph sinuses are only temporary occupants. The third kind of structure within the gland is the trabecular, of which His makes a subdivision under the name of "stroma of the hilus." The trabecular tissue is of a densely fibrillar kind, and forms the capsule of the gland at one pole, the stroma of the hilus at the other, and the true trabeculæ or framework of the gland at all intervening points. The trabeculæ are related to the other structures of the gland in the manner shown in Fig. 19 ; they divide two lymph sinuses from each other ; the fibres that are stretched across the lymph sinus are attached to the follicle or cylinder on the one side of the space, and to the trabeculæ on the other. Like the lymph sinuses themselves, the trabeculæ are of greatest breadth in the medullary or central part of the gland. It is now almost universally admitted that the trabecular tissue, including that of the capsule, contains a certain quantity of involuntary muscular fibre in its substance. The assertion was first made by Malpighi, on what grounds it is not known.† It has been re-affirmed of recent years by Brücke, Heyfelder, His and others on various grounds, such as the isolation by means of nitric acid of highly characteristic muscular fibres, with rod-shaped nuclei, and the frequent occurrence of rod-shaped nuclei *in situ* throughout the substance of the trabeculæ. Frey is of opinion that the latter cannot be distinguished from young or embryonic connective tissue cells. W. Müller, after reviewing all the circumstances, thinks the existence of muscular fibres in the trabeculæ to be probable, but he rests his opinion less on the completeness of the histological evidence than on the fact made out by Brücke and Heyfelder that the lymphatic glands of animals can be made to contract by an electrical stimulus.‡

The distribution of blood-vessels in lymphatic glands.

As regards the circulation through the gland, the afferent lymphatic vessels are known to discharge themselves into the lymph sinuses at various parts of the cortex, and the outcarrying lymphatic vessels to take origin from the wide lymph sinuses in the hilus. The following account of the blood vascular distribution is given by His. Several arterial trunks enter at the hilus ; in the stroma of the hilus takes place the coarser branching ; certain of the branches pass into the trabeculæ ; but the greater number of them pass into the medullary cylinders and run in these towards the periphery into the follicles. The vessel running in the axis of the cylinder gives off many fine branches which open into a capillary network spread out on the surface of the cylinder. Out of this capillary network several small venous branches take origin, which return to the hilus by a venous trunk

* *Stricker's Handbuch*, p. 241.

† His, *Untersuchungen ueber den Bau der Lymphdrüsen*, Leipzig, 1861.

‡ *Henle und Pfeufer's Zeitschrift*, 1863, p. 121.

running along the axis of the cylinder and lying side by side with the artery therein. As to the follicles, they receive their chief arterial supply by extension of the vessels running in the cylinders, and the capillary distribution and venous reflux is on precisely the same system as in the cylinders. In both cases the greatest capillary distribution is on the rounded surface which is directly exposed to the lymph sinus. The lymph sinuses contain no blood vessels.

Recent additions to the histology of the lymphatic glands: the lymph sinuses and their contents.

The most recent additions to the histology of the lymphatic glands concern the lymph sinuses and their contents. The branching fibres that stretch across the sinuses from the follicle or cylinder on one side to the trabecula or capsule on the other have been usually described as branched connective-tissue cells-plates containing nuclei. From another point of view all the nuclear cells that are seen in the lymph sinus have been divided into two classes, those that lie free in the meshes of the reticulum and those that are the fixed cells of the reticulum. Fully accepting the distinction between the two kinds of cells, Bizzozero* has endeavoured to show that the latter are not really the nuclei of branching cell-plates, but that they lie upon the fibres of the reticulum in one or other of two ways: either the fixed cells of the reticulum are thrown round about the fibres, enclosing them as if in a tube of protoplasm, or they are stretched across an entire mesh of the reticulum, like a window-pane in its frame. In the former case the nucleus is seen to lie on the side of the fibre, in the latter case it has a central position in the cell, as in a front view of an endothelial cell. About the same time that Bizzozero made these observations, Ranvier was also led to a similiar conclusion. He also accepted the old division of the cells in the lymph sinuses into two classes, the one being the lymphoid cells whose position in the sinus was merely temporary, and the other being the fixed elements. Of the latter he gave much the same account as Bizzozero had given, but, in accordance with his own peculiar nomenclature, he described them as epithelial cells covering the fibres. It remains to be added that W. Müller had divided the fixed elements of the reticulum into two kinds, one part being mature and the other embryonic. The one were in the form of thin bundles of connective tissue fibres with spindle cells; the other consisted of a delicate finely granular ground-substance (protoplasm), breaking up into a rich network, and with elliptical nuclei embedded in it. Along with the elliptical nuclei there could be observed other and smaller cells which represented all transition stages to the mature lymph corpuscles. Between the numerous irregular openings of this network the lymph current conveyed its fluid, as if, to quote the apt expression of Brücke, through the pores of a sponge.† Finally Toldt has noted the fact that some of the fibres of the reticulum contained nuclei, while others contained none; and has divided the fibres into two classes accordingly.‡

Resumé of opinions as to the function of lymphatic glands.

Notwithstanding the numerous histological researches on the lymphatic glands, their functional import remains conjectural, and in particular the elaborate and beautiful filtering apparatus which is formed by the branching fibres or protoplasmic bands stretched across the lymph sinuses has had no adequate use assigned to it. The oberservation of Leydig,§ to the effect that "the production (*Erzeugung*) of lymph corpuscles is the special physiological task of lymphatic glands" sums up

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* *Moleschott's Untersuchungen*, Vol. xi. p. 300.

† W. Müller, *l. c.*, 126–128.

‡ Eine Methode zur Injection der Lymphbahnen in den Lymphdrüsen. *Sitzungs berichte der Wiener Akademie*, Jan. und Feb. 1868.

§ *Lehrbuch der Histologie*, 1857.

pretty nearly the view that still prevails. In addition to contributing to the number of lymph corpuscles (white blood corpuscles), the lymphatic gland is supposed to purify the lymph in its course through it; but it is not stated what this purification consists in, or in what manner the lymph is at all affected by it. Thus, Virchow* points out that there is no free passage for the lymph through the gland; it must pass between cells more or less closely packed together. The cells of the gland are like the particles of a charcoal filter; the lymph percolates through them and wells out on the other side "as it were filtered and purified." But it need not be pointed out that this is only a graphic illustration, which leaves our intimate knowledge very much where it was before. A more circumstantial account of the function and physiological action of the gland is given by His. The lymph entering the gland by the afferent lymphatics circulates under low pressure in the lymph sinuses and moves slowly therein towards the hilus. The pressure is insufficient to drive the lymph from the lymph sinus into the gland substance. On the other hand, the blood pressure will cause a stream to flow from the highly vascular gland substance outwards to the sinus, and this stream will carry with it, along with the fluid transuded from the capillaries, a number of the lymphoid cells that are being constantly reproduced in the gland substance, and so convey them to the lymph stream. With the contraction of the capsule and trabeculæ, (a rythmical contraction depending on the presence of involuntary muscular fibres in them,) the whole gland seeks to diminish in size, and as the afferent lymphatic vessels possess valves to check a reflux, the lymph sinus will empty itself into the outcarrying lymphatic vessels. At the same time, in consequence of this contractile pressure, the gland substance will for the moment contain less blood. As soon, however, as the contraction ceases, it must happen, in consequence of the sudden relaxation of tension in the interior of the gland, not only that the gland substance will become again richer in blood, but also that the emptied lymph sinus will again become full. The re-filling of the lymph sinus may take place both from the afferent lymphatics and from the gland substance; if the afferent lymphatics contain no lymph, then the lymph sinus is filled entirely by the fluid that has transuded from the gland substance.† One function of the lymphatic glands appears then to be that of adding to the lymph corpuscles of the circulating fluid a certain number more of the same kind derived from the follicular tissue of the gland. Recklinghausen observes that that the reproduction of lymphoid cells in the follicles has in fact never been seen, but that it is indirectly probable for several reasons, the chief of these being that the lymph leaving the gland contains more corpuscles than the lymph entering it.

The facts relating to the waste cells of the mammary secretion place the structure and function of the lymphatic glands in another light.

Returning to the material of this research, we find that we have to deal with factors of a new order altogether, which may or may not be special to the lymphatic glands of the mamma. We have to deal with the conveyance to the lymphatic gland of a peculiar class of cells which are waste products of the secreting gland, and we are concerned not so much with the production of actual new cells within the lymphatic gland as with the changes that it effects upon a certain quantity of cellular material supplied to it from without. Now, it is in this altered stating of the problem that we find some light thrown not only on the function of lymphatic glands but also on their structure. It has been repeatedly mentioned that the large yellow glanular cells which are produced within the mammary acini in certain states of the function, and are often to be seen in the tissues outside, are also found in the lymph sinuses of the lymphatic gland. It is not impossible that an objection

* *Cellular-Pathologie*, p. 208.

† His, *l. c.*, p. 21.

might here be taken as to the actual identity of the cells found in the two situations. It might be said, for instance, that the large yellow cells lose their pigment within the gland, as no doubt they sometimes do, and that the pigment granules are taken up by the ordinary lymph corpuscles that come in contact with them, and so get conveyed to the lymphatic gland. However there cannot be the slightest doubt that the identical cells which are formed in the mamma pass into the lymphatic gland. The size, shape, and general appearance is the same for a great part of those in the lymphatic gland as for those in the secreting gland. But it is not the same for them all. When a tolerably empty lymph sinus of the lymphatic gland is looked at, it becomes at once apparent that the pigmented cells occupy the place of the branched cells of the recticulum; their nuclei correspond to the nuclei of the recticulum, and their pigmented bodies and processes to the expansions and branchings of the same. Fig. 18 is a representation of this appearance. There are in the reticulum no other cells or nuclei, but the pigmented cells and their nuclei; and the only other elements of the reticulum are the fibres. These are fixed structures in the lymph sinuses, and it is contended that they are the only fixed structures. The same opinion might indeed have been arrived at by carrying previous observations to their logical conclusion. Thus Bizzozero, whose theory as to the cells of the reticulum has been given already, states his method in the following terms:—"Concerning the cellular elements of the re-"ticulum—the lymph cells we shall put aside, because in thin sections "they are bound to disappear at the commencement of the shaking—"&c." And again, "The number of the cells (of the reticulum) is "various according to the time that the shaking has lasted. At first "they are present even in grown animals in large numbers, and diminish "considerably the free spaces of the net-work. But the longer the shaking "is continued the more will the reticulum be freed from them, so that "in good preparations one may succeed in making all the cells to dis-"appear, and the reticulum to appear quite naked." The fallacy in this method is palpable. The cells that are first dislodged by the shaking are lymphoid cells; the cells that are afterwards dislodged are the cellular elements of the reticulum. All the cells adhere to the reticulum more or less, but they can be all dislodged by shaking the sections. At a particular point in the shaking process, the lymphoid cells have been got rid of, and the cells of the reticulum remain. But it is quite arbitrary to call the first sort lymph cells and the others the cells of the reticulum. If the distinction means anything at all, it means that the so-called cells of the reticulum are the cells of the lymph sinus that adhere most closely to the fibres of the reticulum. It must be conceded, however, that the so-called cells of the reticulum have certain differences in form. Many of the large yellow granular cells in the lymph sinus are of their usual round form, but many of them—and in the emptier lymph sinuses the whole of them—are either drawn out into processes which follow the direction of the fibres, or they are otherwise stripped of their protoplasmic cell substance and their pigment, in all degrees down to the condition of naked nuclei. The various steps of the process by which the cells lose their protoplasm and their pigment in the meshes of the reticulum are so clear that the fact in its entirety becomes well established. For example, a large yellow granular cell with visible nucleus has its substance drawn out into two or three or four processes which correspond to the direction of fibres running between the trabecula and the cylinder. Again, a row of free pigment granules is seen to be the continuation of a somewhat truncated cell process, the granules lying in or upon the fibre. Again, the pigmented cell is found stripped of all its cell substance except a mere yellow fringe round the nucleus. Lastly, from another

Argument that the lymph sinuses contain no fixed cells or nuclei.

The waste cells are reduced to the condition of nuclei in the lymph sinuses.

point of view, nuclei are constantly met with which have a few granules of yellow pigment clinging to them. Those are a few examples of the transition appearances of the large pigmented cells in the course of losing their pigmented cell body.

The mode of their reduction.

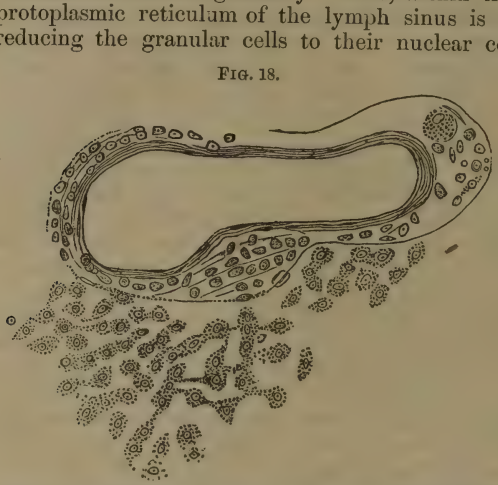
The next question that arises is the manner in which the denudation takes place, or the part that the so-called fibres of the reticulum play in the same. Reference has been made to the discovery by Wilhelm Müller of two kinds of substance composing the reticular meshwork. One kind he describes as the ordinary connective tissue bundles containing the ordinary spindle cells; the other kind was a delicate finely granular protoplasmic substance which contained large elliptical nuclei, and broke up into branches. Along with the elliptical nuclei he found in the protoplasmic substance a number of smaller cells showing all gradations from the large elliptical cells down to the ordinary lymphoid cells of the follicles. The small cells he attributed to a proliferation of the nuclei at the spot, and he figures certain appearances of clusters of nuclei which seemed to point to a process of cell division. The same protoplasmic condition of the reticulum and the same varieties of cells in its substance are also recorded by Frey in his text-book, and the figure given by the latter (Fig. 389) is in the highest degree confirmatory of the view that is now to be stated of these appearances. Frey mentions incidentally that he had seen the same protoplasmic meshwork in the lymph sinuses of the mesenteric glands, and that he had seen the fat molecules of the chyle within them; but he adds that he then made the mistake of supposing the reticulum to be "a system of cellular tubes." The true explanation seems to be not that the reticular substance is a fixed system of tubes, but that it can be made tubular by cells passing into it. There is often to be seen, in the course of a fibre, the appearance of a sudden hollow expansion within which lies a nucleus. The outlines of the expansion usually taper abruptly, and become continuous again with the narrow fibre beyond; but sometimes the breadth of the fibre beyond the nucleus is hardly less than at the point of expansion. In one of the preparations of the series there was seen a long "fibre" of the lymph sinus which had no fewer than three separate dilatations on it, each containing a round nucleus, while there seemed to be a free passage in its substance between them. The appearance was very like the beaded condition of a double-contoured nerve fibre. Whatever may be the exact process, there is no doubt that the large yellow granular cells become entangled in the meshwork of the lymph sinus, and thereby lose their pigmented protoplasm. In all probability they travel through a considerable length of sinus, and come in contact with the reticulum many times before they are reduced to their nuclear condition. The disposal of them after this point falls to be considered separately. The use of the lymphatic gland may be compared not so much to that of a charcoal filter, as to the double purpose of a winnowing fan. In the first step of the process the husk is loosened and detached from the grain or kernel, and in the second step of the process the useful elements are separated and collected together. But even this illustration does not exhaust all the changes effected by the lymphatic gland or the cells that pass through it. There are, however, some other appearances to be described before we come to amplify that illustration.

The waste cells may pass direct into the follicles or cylinders.

In the accounts of the involution and evolution process it was stated that the large yellow granular cells were sometimes reduced to the nuclear condition, with loss of their pigment, while they were still in the mamma. Collections of them can be seen in the fibrillar tissue which show very much the same gradation from the full-sized nucleated granular cell to the naked nucleus, as has been described for those in the

lymph sinus of the lymphatic gland. Again, in the final state of involution, the contracted acini are found to have a few grains of pigment lying free among the resting cells, and in some cases where the free pigment is not seen in the acini it may be seen strewn over the surface of the lobule generally. Now, within the lymphatic gland, the protoplasmic reticulum of the lymph sinus is not the only agency for reducing the granular cells to their nuclear condition. Fig. 18 is a drawing from the case in which the lymphatic glands beneath the mamma were in a rudimentary condition; that is, the follicular tissue was at its lowest point, while the lymph sinuses and the stroma of the hilus were of great extent. The figure shows the section of a large vein, and the follicular tissue is represented by two or three rows of lymphoid cells in its adventitia. Surrounding the vein with the lymphoid cells in its adventitia is the large lymph sinus filled with pigmented cells, many of which are drawn out into processes, as already described, while some of them have their cell substance reduced in amount. It will be observed that the lymph sinus is separated from the rows of lymphoid cells by a membrane, which is, as it were, the outermost layer of the loose adventitia of the vein; it appears in the figure as a dark line. Now, this limiting membrane showed in the coloured preparation an interesting condition of things which could not very well be transferred to the figure. It showed at one or two points a pigmented cell as if adhering closely to it, drawn out to a long narrow form, and with its pigmented granules scattered along the outline of the membrane for a considerable distance on each side of the cell mass. The cell was no doubt passing from the lymph sinus into the follicular area, and losing its pigmented substance in the process. In the preparations of the same case another very definite appearance is often to be seen. In parts of the gland where the follicles are of considerable size, the surface of the follicle is strewn with numerous grains of pigment approaching to red in colour. These grains are sometimes of considerable size, circular, and with the characteristic dark border. The lymph sinus surrounding the follicle is full of the ordinary yellow nucleated cells; the pigment of the latter is much paler than that strewn over the follicle. The collections of the darker coloured free pigment are limited exactly to the follicular tissue. The inference seems to be that some of the cells enter the follicles with their pigmented substance, or at least a portion of it, still adhering, and that the pigment which they lose there is not at once carried away, as it would have been if the denudation had taken place in the sinus through which the lymph current is passing. There is one more mode of reducing the granular cells to a nuclear state, which has something of a phenomenal or exceptional look about it.

Fig. 18.

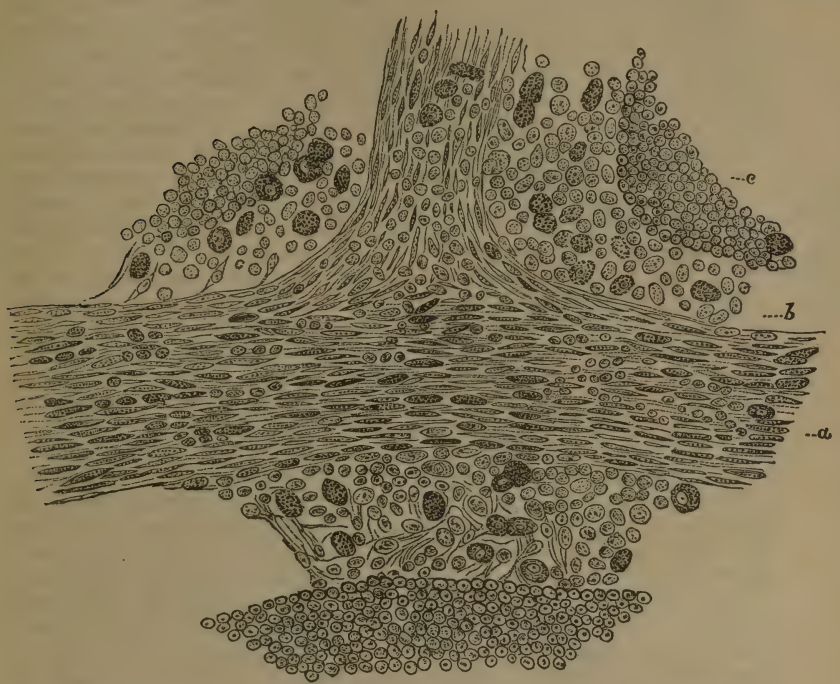


From a lymphatic gland beneath the mamma. The follicular tissue represented by two or three rows of lymphoid cells in the adventitia of a large vein; the lymph sinus occupied by *large yellow cells* with their substance often drawn out into processes. Magnified 300 diameters.

The waste cells may penetrate into the substance of the trabeculæ.

It is represented in Fig. 19, which has been drawn as accurately as possible. The lymphatic glands are those from beneath the mamma in

Fig. 19.



From the medullary part of a lymphatic gland beneath the mamma of a cat: *a*, trabecula crowded with spindle cells, some of which have the same substance as the large dark cells in the lymph sinuses (*b*); *c*, portion of a lymphatic cylinder. Magnified 300 diameters.

the same case from which Fig. 14 is taken. The latter shows abundant production of the yellow granular cells in the mamma. Now the lymphatic glands did contain traces of yellow pigment, but the large nucleated granular cells that were found in the lymph sinuses were not of a yellow colour, but stained very dark by the colouring reagent (logwood). Their granular character is more distinct than in the case of the yellow cells, and they have often the mulberry surface. In other respects they are exactly the same as the large yellow cells. They have been found in the mammary lymphatic glands of two other cases slightly more advanced in evolution, and in the special case, several times mentioned already, of a lymphatic gland made up almost entirely of lymph sinuses and pigmented cells in them, they were found here and there among the ordinary yellow cells. There is no doubt that they are only a modification of the large yellow cell as regards its pigment, and it may be that they represent the waste product of a somewhat later stage of evolution. The portion of gland drawn in the figure is taken from medulla not very far from the hilus. Portions of three cylinders of the medulla occupy the outer parts; next to them come the corresponding lymph sinuses, and in the centre running horizontally, is a broad trabecula with an extension upwards. The lymph sinuses show indistinctly the fibres of the reticulum, and they contain, besides a number of the large granular cells, many nuclear cells of various sizes. If the trabeculæ are examined, they are found to present a most extraordinary appearance. They are crowded with staff-shaped or

spindle-shaped cells (or nuclei), which follow with their long axis the direction of the trabecular fibrils. About one fourth of the elongated bodies have the intensely dark granular appearance of the large round cells in the sinus, and these are also the largest and broadest; the majority of the elongated elements are narrower, pale, and granular, and there are transition stages as regards depth of staining and shape between those two kinds. The contention is that the elongated cells in the trabecula have penetrated from the lymph sinus, and have acquired their shape from passing through the narrow inter-fascicular spaces. No other explanation of the *tout ensemble* of this picture suggests itself. The staff-shaped nuclei, if not the spindle-shaped, have often been seen in the trabeculæ of lymphatic glands, though they do not appear to have been figured before in such numbers or in such variety. The usual account of them is that they are the nuclei of involutary muscular fibres; but it has been pointed out already that some authorities are not satisfied with the histological evidence for this allegation, and that W. Müller, an impartial critic, is led to accept the theory chiefly because the lymphatic glands have been shown to contract under an electrical stimulus. Now there is no motive whatever in the present research to explain away the presence of unstriped muscular fibre in the trabeculæ of lymphatic glands; the subject may be said to have cropped up accidentally. But it seems a most unlikely thing that a certain number of these spindle-shaped or staff-shaped nuclei should be, as their granular substance and the colouring shows them to be, cells that have penetrated from the lymph sinus, and that a certain number of them, not marked off from the former by any rigid line, should be the nuclei of involuntary muscular fibres. Other observers have pointed out that many of the alleged muscular nuclei have not the appearances of these latter at all, but are more like the nuclei of embryonic cells; and the writer has in his possession preparations from the mesenteric glands of the ox, hardended in bichromate of potash, which show part of the trabeculæ or capsule to be crowded with round and elliptical nuclei, and without a single staff-shaped nucleus among them. Again, large tracts of trabeculæ may be seen without any nuclei at all, and, in fact, in text-books the trabeculæ are generally so figured. The settlement of this question depends, in the last resort, on whether "highly characteristic" involuntary muscular fibres have actually been isolated.

Argument that the so-called muscular nuclei of the trabeculæ are not fixed elements of the trabeculæ.

What then, it will be asked, is the further course of the cells that have penetrated into the trabeculæ? If the course of a trabecula is followed in sections of the gland, it will be found to narrow to a point where the sinus bends, and to break up into a sort of brushwork of fibres, which are the ordinary fibres of the lymph sinus. The stream of elongated nuclei in the trabecula is continuous with the round nuclei in the protoplasmic reticulum. At all parts of the trabeculæ, the bands or fibre stretching across the sinus appear to be nothing else than detached portions of the former. They arise from the side of the trabecula at a more or less obtuse angle, and when the trabecula appears in the section to come to an end, they form the brush-like continuation already described. Finally, if the bands and fibres of the reticulum have the highly plastic or protoplasmic character that they are alleged to have, so no doubt have the more compact fibres of the trabecula; and that fact would perhaps account for their contractility under an electrical stimulus without supposing them to contain muscular fibres.

The correctness or incorrectness of the explanation given of the staff-shaped and spindle-shaped cells in the trabeculæ in Fig. 19 has an important bearing on the question already raised with reference to Fig. 16. The latter is held to show a particular form of the waste products of evolution on their way through the interfascicular spaces of the mam-

mary interlobular tissue, and the exactly analogous occurrence in the trabecular tissue of the lymphatic gland may be held to place that view beyond doubt. If the connective-tissue theory in the one case, and the theory of involuntary muscular fibres in the other had not been already in possession of the field, it would have been hardly necessary to argue the question at all.

Up to this point we have found one function at least of the mammary lymphatic glands to be the reduction of the granular waste cells of the secretion to the status of nuclei. We have seen that such denudation takes place chiefly among the protoplasmic fibres and bands stretched across the lymph sinuses, but that a similar change is effected on the large waste cells in their passage through the limiting membrane of the follicle or cylinder, or in their passage through the interfascicular

The origin of the follicular tissue of the lymphatic glands.

Fig. 20.

From a lymphatic gland (same case as Fig. 18). In the centre of the figure, the longitudinal section of a vein which discharges below into a larger vein; the follicular tissue is represented by rows of lymphoid cells in the adventitia of the vein, and especially of its branches; the lymph sinuses are filled by *large yellow granular cells*. Magnified 150 diameters.

spaces of the trabeculæ. The special use or significance of the follicular tissue of the gland has not yet been touched upon, and although that is a more difficult point than the preceeding, some of the preparations of this series are not without instruction as to it. The Fig. 20 (p. 167) is taken from a case already referred to. The lymphatic glands were quite small bodies in the midst of the cushion of fat beneath the mamma in the inguinal region. They seemed to the naked eye to be composed almost entirely of yellowish pigmented material, which was found to be the waste material of the secretion; and it appeared as if the conveyance of so large a quantity of waste cells to a particular point in the fat tissue beneath the mamma had given occasion for a lymphatic gland to develop itself, its framework being derived from certain fixed elements of the part—blood vessels and stroma—and its parenchyma being formed by the waste material in its crude or in its subsequent transformed state. Now, whether or not a set of lymphatic glands may have at one time existed only *in posse* at that part of the fat tissue, it does appear from the examination of the glands as they were found, that their chief and earliest constituents were the dense and abundant stroma of the hilus, the large lymph spaces, and the blood vessels. The glands were in fact rudimentary glands, and that not in the sense of embryonic development, but in the sense of an old and disused function being suddenly revived. The animal was aged; and the great production of waste cells, though it followed in the track of evolution, was not actually due to the ordinary cause of evolution, but to some unknown pathological excitation. If the drawing is referred to, it will be seen that the dense fibrillar stroma of the hilus is the most abundant tissue; that it is penetrated in various directions by wide lymphatic spaces, the lymph sinuses; and that the follicular tissue is represented only by one or more rows of lymphoid cells in the walls of the veins. One of the latter is shown in longitudinal section with several branches. Beginning at the top of the figure, there is seen at the left-hand corner a considerable follicle or cylinder, in the centre of which is a vein. On the other side at a corresponding point, there is another cross section of a vein with a smaller number of lymphoid cells round it, and if the longitudinal vein is traced downwards, it will be seen that the lymphoid cells which form two or three rows at its upper part and round its branches, diminish in number at its lower part, and, where the vein opens into the large venous trunk at the bottom of the figure, are altogether wanting. The figure is nothing less than an objective demonstration of the plan of a lymphatic gland on a small scale. The blood vessels have long been known to run in the axis of the lymphatic cylinders, and Billroth* in 1858, suggested what is undoubtedly the true account of the relation of the lymphoid corpuscles to them. He described the cylinders of the gland to be simply the loose adventitia of the blood vessels containing lymph. This view of the matter at once places the follicular tissue of the lymphatic glands in the same category as the follicular tissue of the spleen. Following the summary of Hermann,† the Malpighian bodies seated on the fine arterial twigs are to be considered as true lymph follicles (Gerlach); they form circumscribed thickenings on the walls of the arteries, and are to be viewed as simple deposits of colourless cells (lymph cells) in the interspaces of the adventitia. In many animals the alveolar thickenings are not circumscribed, but are more uniformly distributed over the arterial wall (W. Müller). It is to be noted that in the spleen the collection of lymphoid cells takes place in the walls of the arteries, and that in Billroth's account of the lymphatic glands, the arteries and veins are not

The lymphoid cells are contained in the adventitia of the veins.

Analogy between the follicles of lymphatic glands and the follicles of the spleen.

* *Beiträge zur pathol. Histologie*, Berlin, 1858.
† *Grundriss der Physiologie*, p. 175.

spoken of separately, but "the blood vessels" in general. In all the preparations of the above case it appeared to be the adventitia of the veins in which the lymphoid cells almost always reside; although a few lymphoid cells were sometimes to be seen in a row round the lumen of an artery. So much, then, for the relation of the trunks of the vessels to the lymphoid cells of the gland cylinders; the cylinders of the medulla are essentially their loose adventitia filled with lymphoid cells. When we come to consider the follicles of the cortex, Brücke's* reading of the structure of the latter proves serviceable. The medullary cylinders contain all the larger blood vessels, which are provided with stout adventitia; a portion of their branches break up into capillaries on the cylinders, and the rest proceed to the cortex of the gland. The further removed from the large vessels, the looser does the connective tissue of the adventitia become, and at length there appear, in the place of connective tissue fibres, "cytoblasts" whose cell membranes enclose narrow spaces, and which are provided with two or three thread-like processes. They have been drawn out (*verfilzt*) into a soft felt-like tissue in which the blood capillaries tie. Innumerable fine passages lead through this tissue and make it porous, like a sponge. Several theoretical emendations might be suggested to this account, but it will at least serve as the basis of the statement that the small-meshed reticulum of the follicles is simply a modification of the adventitia of the vessels that enter them. At the same time we have seen in these preparations that the smaller the vein is, the larger is the collection of lymphoid cells in its wall. As we approach the cortex or periphery of the gland, we find that the adventitia of the vessels is frayed out into a spacious meshwork, and that the lymphoid cells are now so numerous as to fill it.

Some facts have been mentioned already to show how the waste cells are denuded of their substance and pigment in passing from the lymph sinus into the wall of the vein, *i.e.*, the follicular tissue; and it is not difficult to make out that the cells that have been reduced to the nuclear condition in the lymph sinus itself, or in the substance of the trabeculæ, must enter the cylinders and follicles in much the same way. This brings us to consider what is the further effect of the lymphatic gland on the waste cells brought to it, besides the two uses of it which have been compared to the double purpose of a winnowing fan. The lymphatic follicles no doubt represent the heaps of cells that have been cleared of their pigment and granular investment; the follicles are a sort of reservoir in which they collect, and from which they may be again swept out into the lymph current, in the manner described by His, and quoted on p. 161. But they have evidently another purpose. The meshwork of the follicle differs very much from that of the lymph sinus; the meshes are very much finer, and they are of a uniform size. Now, if the lymph sinus in Fig. 19 is examined closely, it will be seen to contain some very large nuclei, and some of the ordinary lymphoid size; the large nuclei have a distinct linear contour, a pale homogeneous substance, and a comparatively large nucleolus. Where they come from in this particular case belongs to a former part of the inquiry; they are probably the characteristic waste products of the middle period of evolution. Now the lymphatic gland effects a change on those cells also. They may be seen in the interior of the trabecula, and very often along its edge, as if in the outermost interfascicular space. Before they emerge from the trabecula they must be presumed to have suffered very considerable compression. The permanent compression of a cell into a smaller bulk, accompanied with a condensation of its substance, is a

The waste cells are reduced to a uniform size in the meshes of the lymphatic follicles.

* *Ueber die Chylusgefässe und die Resorption des Chylus*, p. 34–35.

notion that cannot be supported by quotations from independent writers; but it is not at all against the analogy of plastic material in general, and as a matter of fact, the smaller round nuclei do appear to be of more dense substance, if the depth of their staining is any criterion of the matter. It may be said of lymphatic glands in general that the cells in the lymph sinus are not only fewer than those in the follicles and cylinders, but that they are also a size larger and that their substance is paler. But even within a follicle a corresponding difference may be seen now and then. Some of the follicles in these same preparations are seen to have their periphery composed of two or three perfectly regular parallel rows of small and deeply stained lymphoid cells, while their central area is much paler and filled with cells that appear to be of a larger size and are less deeply stained.

The conclusion is that the cells entering the follicle pass through it in more or less regular order, and that the purpose of the fine meshwork through which they are passed is to reduce them all to a uniform size. It is not asserted, however, that all the cells in the lymph sinus leave the lymph current and enter the follicle.

We have thus followed, step by step, the evidence to show that the waste cells of the mamma enter the special lymphatic glands of the organ, that they undergo various degrees of change according to their requirements, and that they do not leave the gland till they have acquired a uniform size. The finishing touch of their reduction takes place in the follicles, and from these they issue on a new career. All that has been asserted of the follicles as matricular organs for the production of lymphoid cells may be asserted of them, *mutatis mutandis*, as organs for the final moulding of the same. In both cases, they must be held to supply new elements to the blood. It might very well be made a question whether the whole of the new supply of cells is swept out of the follicles into the lymph sinuses as His explains, and is so conveyed to the blood current after a long course through other lymphatic glands. The capillary distribution in the follicle seems to offer an opportunity for the cells of the follicle to enter the circulation at that point, and in more than one of the cases used in this research, the vein leaving the lymphatic gland has contained in the section a very large number of colourless cells.*

The waste cells after passing through the lymphatic glands, are utilised as white blood corpuscles.

This utilization of the waste products of the mammary secretion naturally implies a large addition to the number of white corpuscles in the blood; and such an increase is actually found to take place during pregnancy. The subject attracted the attention of Virchow at an early date and is discussed in his *Gesammelte Abhandlungen*. In the *Cellular Pathologie* he describes it as a case of physiological leucocytosis. In his earliest notice he pointed out that those periodical changes of the blood did not take place within the blood itself; the cause of them lay without, and he specially mentions "organs of secretion and reception, "but especially the proper matricular organs of the blood, among which the "lymphatic glands must be placed first."† In the *Cellular Pathologie* the subject is noticed as follows: "In proportion as a pregnancy advances, "as the lymphatic vessels of the uterus enlarge, as the *Stoffwechsel* "in the womb increases with the development of the fœtus, the "lymphatic glands of the inguinal and lumbar regions get considerably "enlarged, and sometimes to such an extent that if we found them at

* This is mainly theoretical ground, and the theory may be carried a step further. The lymphatic follicles might be regarded as places where a white blood cell from time to time may leave the circulation, undergo a purification or rejuvenescence, and again return to the circulation.

† *l. c.* p. 760. H. Hasse is quoted by Virchow as a prior authority.

"any other time we should say they were inflamed. This enlargement "brings to the blood still more new particles of a cellular nature, and "so the number of colourless corpuscles rises from month to month."* The process described in this report may be taken to supply some of the particulars for Virchow's general account; and if, as seems likely, an analogous process takes place in the uterus throughout the same period, we might be able to trace the physiological leucocytosis of pregnancy to another of its great sources. As to the fact of a leucocytosis in the animals used in the study of the evolution of the mamma, the observations were not conclusive. The point was neglected in the earlier cases, and in only two of the later was the increase of white corpuscles very marked. In both of these there were from 30 to 50 in the field of the microscope.

The leucocytosis of the pregnant state.

There is another class of appearances in pregnancy, besides the leucocytosis, on which the study of the evolution of the mamma throws some light. These are the peculiar deposits of pigment. Many of them, especially those that occur in women along the lower part of the linea alba, are perhaps to be referred to the uterus, in which we have seen from a case in the cat that there is pigment formation, at least in involution. The pigmentation of the areola, on the other hand, may be referred directly to the pigment production within the mamma during evolution. It is obvious that if the pigmented cells in Fig. 13 travelled along the submucosa of the ducts all the way to their orifice, instead of breaking into the lumen, they would form a deposit of pigment in the areola. The acute observation of Sir James Paget that a pathological cellular process in the areola is often found to precede, at least to the observer's eye, the formation of a cancer of the breast, may be capable of explanation in the same way, looking at the cells rather as waste cells that have travelled thither, than as the carriers of pigment. But to go into that point here would be to anticipate many facts and arguments that have to be stated systematically and in due order in the pathological part of the report.

Pigmentary deposits of the pregnant state.

Section IV.—A preliminary Notice of some Points in the Development of the Mammary Gland in the Embryo.

The development has been studied in the fœtuses of the cat and guinea-pig. In the almost full-grown fœtus of the cat there is found in the inguinal region a pair of lobulated parenchymatous bodies, of the relative proportions and position of the future mammæ, when these are limited, as in the guinea-pig, to the extreme lower part of the abdominal wall. These bodies are not the mammary glands, but fat-bodies, of the kind well known in insects,† and which have been described by Toldt ‡ as occurring in certain mammalian animals at birth and in batrachians in the adult state as well. Toldt has already described this inguinal fat-body in the cat, but he has not found out its peculiar significance. If a section of it is made and examined with the microscope, it is found to be divided into lobules, like an acinous gland, and to have a rich vascular supply. Each lobule is is made up of a heap of large granular cells, all

The rudiment of the mammary gland is a fat-body.

* *Cellular Pathologie*, p. 229.

† See Leydig's *Lehrbuch der Histologie*, p. 341. In the firefly the substance that emits the glow consists of mineral particles within the vacuoles of the cells of the fat-body. Leydig states that the situation of these particles strongly suggested to him the concretions that are found in the vacuolated renal epithelial cells of molluses.

‡ Beiträge zur Histologie und Physiologie des Fettgewebes. *Sitzungsb. der Wien. Akad*, Juli, 1870.

of which show the most exquisite type of vacuolation. The cell substance forming the wall of the vacuole is considerable in amount, and has at one side a nucleus embedded in it. Now if this body is examined in sections passing through it in all directions, nothing but the same appearance of large granular vacuolated cells is found; there is not a trace of the characteristic mammary structure. But in animals a few days older, as in the guineapig two or three or four days old, a change is found to have occurred. The whole of those lobules of granular vacuolated cells have become the ordinary fat cells, as described by Toldt,—except over a certain area of the fat-body on the upper surface at its anterior end. At that point there is found a small firm mass of tissue with lines or tracts of the same running for some distance through the fat. On examination of this area, the rudiments of the gland are found, and the parts of it that correspond to the acini seated on the ducts show the following appearances. They are somewhat large circular areas about as large as a fully expanded acinus of the adult, and they are filled with a number of large vacuolated cells. At the very first glance, one can identify many of those cells with the vacuolated cells of the fat-body as already described; they are the same in size, they have the same granular protoplasm, which contains at one side a nucleus embedded in it. Many of them, again, are more extensively vacuolated, and are reduced almost to the condition of delicate rings from which the nucleus is more or less detached. The acini and the ducts on which they are seated contain a fatty fluid.

A portion of the fat-body becomes the mamma, while the greater part becomes the ordinary fat tissue that surrounds the mamma.

The explanation of the appearances is as follows. About the time of birth the greater part of the vacuolated cells of the fat-body become more extensively vacuolated and form ordinary fat cells. A certain number of them, however, at the upper side of the anterior end of the body, get portioned off into round groups. Within these groups the vacuolation takes a different turn. Instead of the fatty fluid of the vacuole remaining inside it, as in the fat cell, it is discharged as in the formation of milk. The cell has been at the same time less extensively vacuolated, and the peripheral nucleus remains of a considerable size. The vacuolated cells are ranged more or less regularly round the wall of the round space; the vacuoles break up and disappear, and their nuclei remain. The round spaces, which were at first as large as a perfect acinus, then contract, and the nuclei are retained within them as the rudimentary epithelium of the gland. The oily substance produced from the vacuolated cells in the round spaces is the milk of the new born or "hexenmilch." It could be expressed from the teats of a guinea-pig two days old, and it was found on examination not to contain the ordinary globules of milk, but to be in the form of large and irregular drops of an oily substance, the particles of which had no individuality.

The origin of the milk of the new-born.

Earlier stages of the fat-body.

Tracing the fat-body further back in the development, beyond the stage of fœtal life at which it is first mentioned here, it is found to be in the form of more or less isolated lobules of cells in the lower layer of the corium. Those lobules are highly vascular; the cells composing them have often the appearance of the epithelial-like cells of the suprarenal body. The earliest appearance of the lobules is found to be small scattered collections of cells in the same region, grouped round about the vessels. Many of these had the appearance of having given origin in their interior to the red blood discs that lay near them, and others appeared to contain in them a brownish or orange-coloured fluid; they are probably of the same kind as the blood-forming cells which were found by Schäfer * in the connective tissue beneath the skin of the

* *Proceedings of the Royal Society*, No. 151, 1874.

back in young rats. Both Toldt and Flemming* have described the grouping of the young fat cells about the vessels, as they are here seen.

Many details of this discovery remain to be worked out, but the facts above given are correct, and they are indirectly confirmed by an observation of Kölliker's that the "formation of cavities in the rudiment of the "mammary gland is accompanied with the formation of fat-containing "cells in their interior;" and he correctly points out that the milk of the new-born is the fatty substance contained in these cells.† But he makes no mention of the gland developing in the midst of a fat-body and as a modification of a part of the same. The explanation now given cannot fail to strike the reader as being singularly in accordance with the view that has been independently formed as to the law of the mammary secretion. The final step in the development, which has been chiefly dwelt on here, is, as it were, an isolated act of secretion, and its secretory product is the milk of the new-born which lasts for a day or two only. The developmental excitation is the same as the secretory excitation, which reappears in the female only, and after a long interval. The cellular activity in both processes comes under the law of endogenous cell formation.

The last step in the development is the same cellular process as occurs in the adult secretion.

Part II.—Pathological Processes of the Mamma.

In the foregoing part of this report there has been given what claims to be a full account of the various processes or modes of activity that go on in the female mamma during the maturity of the individual. It is by means of this *apparatus physiologicus* that the elucidation of certain common diseases of the organ is to be attempted. These are the more ordinary tumours of the breast.

First among the physiological points that have been dwelt on is the fact of the periodical evolution and involution of the gland. No other organ of the body, except the uterus, is subject to periodical changes of the same kind. The function of the breast intermits regularly for a longer or shorter period; its subsidence is gradual, and its re-establishment very much slower. In both of those processes the ordinary functional excitation of the gland is still present, but it acts at a lower degree of intensity, gradually decreasing to complete cessation in the involution, and gradually rising to its full force in the evolution. In those two inverse processes there is a complete parallelism. They may be both divided into tolerably definite stages which correspond exactly in an inverted order. The stages are characterised by secretory products of the epithelium peculiar to them, and the peculiar secretory product of each stage, occurring as it does at corresponding periods of both processes, may be considered to be the characteristic product of the excitation of the gland acting at a certain absolute degree of intensity. When the functional stimulus of the mamma is acting at its lowest point, the secretory product is a large granular pigmented cell; if the mammary excitation were always to act at that degree of intensity, the secretion, it may be said, would be always in the form of large granular pigmented cells. At the next appreciable advance in the intensity of the stimulus, the product discharged from the gland may be described somewhat generally as a large nucleus. Beyond the medium degree of intensity, the product is both fluid and cellular, the former being mucus

Summary of the corresponding stages in involution and evolution.

Arhiv für microscopische Anatomie, Vol. VII., p. 65.

† *Entwickelungs-geschichte*, p. 345.

and the latter, generally speaking, a small round cell. Coming still nearer to the full excitation, the cellular ingredients are fewer and the mucous production much more abundant. Finally, when the stimulus is at its height, the mucous fluid has given place to a fatty fluid, and whatever cellular elements the secretion contains are the well known colostrum cells. This summary will be found to be strictly in agreement with the facts already detailed at length. It is submitted once more that the parallelism between the involution and evolution processes is not at all strained, and that it is a quite legitimate inference to ascribe, in the abstract, a special kind of secretory product to a certain degree of intensity of the glandular force.

The various cellular and fluid products of the imperfect secretion are spoken of as waste products. The various healthy modes of their disposal have been described at length. Lastly, the law of the secretion, the *modus operandi* which is at all times implicitly present, and which is clearly manifested in the imperfect states of the function, is the law of endogenous cell formation. So far the physiological processes of the mamma have been expounded ; but in passing to consider its diseased processes, there remains to be added another physiological consideration which has been deferred till now.

The special property of cells produced endogenously.

The morphological differences between the endogenous mode of cell formation and the mode by division have been already referred to ; and the point that has now to be stated here has also been dwelt on at considerable length in the previous report on the Ætiology of Cancer. The mode of cell formation by division is essentially a partitioning of the whole cell into several fractions, which grow and acquire the same characters as the cell from which they came. This is the kind of cellular activity in all processes of growth. In the endogenous mode the new cell tends to be rounded to a separate whole within the vacuole of the parent cell. This is the form of cellular activity in the processes for the propagation of new individuals.* The former mode of cell formation is the hyperplastic, and to the latter Virchow has given the convenient name of metaplastic. The property, then, of metaplasia may be said to inhere in all cells produced according to the law of endogenous cell formation ; and if we are content, for brevity's sake, to use a formula for the expression of those complicated processes in the breast that have been previously described, we are at once led to the conclusion that all the cellular products of the secretion, or, in other words, the waste cells of the secretion have the same property of metaplasia. It is in this property of metaplasia that their importance as regards disease chiefly consists. For metaplasia is nothing else than the heteroplasia which we uniformly associate with the "parasitism" or malignancy of tumours.

The material used in the pathological study.

The material used for studying the pathological processes in the breast consisted of 9 cases of mammary tumour from the human subject, 8 female and 1 male ; 16 cases of mammary tumour in the bitch, several of them multiple ; and 2 cases in the cat. The human cases were fairly representative of the varieties of hard and soft cancer. They occurred, all except one, in the surgical practice of St. Thomas's Hospital, and were obtained for the purpose of this research through the courtesy of members of the surgical staff. The two cases in the cat were precisely alike ; they correspond most nearly to *Carcinoma reticulare*. In one of them the disease extended over a considerable part of the chain of glands on one side ; in the other case, where the tumour was more circumscribed, a large tumour grew in the axilla after the removal of the primary tumour, and there were found also numerous

* Sachs, *Lehrbuch der Botanik*, p. 8–9.

secondary nodules in the lungs. Those two cases, as well as the 16 cases in the bitch, were under treatment at the Brown Institution, London, and the material was obtained for examination under the most favourable circumstances through the great kindness and assiduity of Mr. William Duguid, the veterinary surgeon of the institution. The cases in the bitch had several points peculiar to them. In rather more than one third of them there was a tendency to the formation of cartilage at certain points, and a large part of the principal tumour in one of the cases was distinctly osteoid. The most common feature of the tumours in the bitch was their tendency to myxomatous transformations, of which the cartilaginous tendency was in some cases a further development. In one case, which had secondary tumours in the liver and lung, the superficial part of the mammary tumour was occupied by a large cyst containing colloid fluid. In two or three of the tumours the appearance was very much that of skirrhus of the human breast, except that the juice was brownish. Some of the cases, however, had nothing of the myxomatous appearances, but resembled rather the kind of structure found in the tumours of the cat; and, in particular, one case occurred of a large soft tumour, which corresponded, in minute structure as well, to the "medullary" cancers of the human breast. Several kinds of structure were often found in the same case. Thus, in an extensive tumour that recurred after removal 18 months before, there were found several small areas of well developed cartilage; elsewhere the structure was of somewhat soft consistence, and the lungs were found to contain numerous soft white secondary tumours. Thus, although the mammary tumours in the bitch showed a decided tendency towards the comparatively safe cartilaginous transformation, there was no reason to consider them as a class other than malignant tumours. They were sometimes multiple, they had a tendency to recur, they increased by extension into surrounding tissues, and they produced secondary affection of the lymphatic glands, liver, and lung. They occurred for the most part in aged animals, and only one of the cases was known to have been never in young. Information as to heredity could not be got; but it is well known from other sources that tumours in the dog are very liable to be inherited, though the same kind of tumour is not always transmitted.

Opportunities of studying the initial stages of tumour formation.

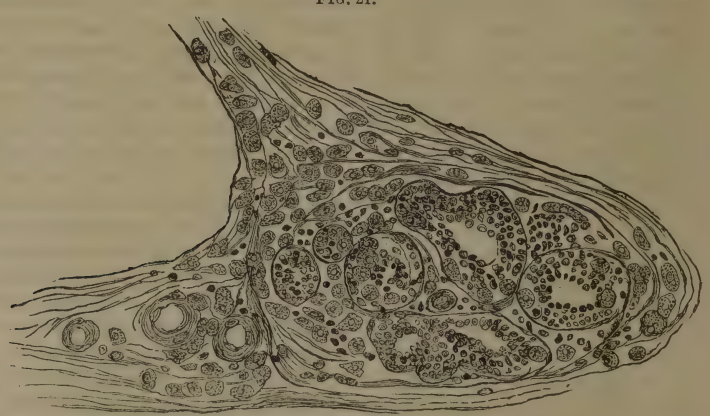
In the cases where the tumours were multiple, there was generally one large tumour, with several smaller situated at intervals along the chain of glands. The small tumours were found not unfrequently to represent an earlier stage of the disease. Again, there was found in one case a still more instructive condition. In addition to one large tumour, there were numerous small circumscribed tumours throughout the entire extent of gland substance on both sides; and, at one part, there was over an area two inches square, a uniform enlargement or thickening of the gland. Over this area the gland was $\frac{3}{8}$ to $\frac{1}{2}$ an inch thick, and was the subject of the diseased process in an early stage. The initial stages of the disease could be seen more or less clearly in most of the cases. In several of them the entire chain of mammary glands was obtained for examination, and in all the other cases except one, considerable fringes of the mamma were found round about the tumour. Those fringes of mammary tissue, though less in extent, were hardly less valuable for the pathological inquiry than the entire chain of glands would have been. Thus, from the more or less normal mamma to the small circumscribed tumours and to the principal tumours there appears to be a gradual transition. Whether the diseased process is throughout one and the same is entirely a matter of observation, and, in what follows, the question will be so treated.

The attempt to refer the tumours of the breast, whether in the human subject or in animals, to their respective classes, is deliberately abandoned as serving no good purpose. It will doubtless be found to be more in keeping with the ætiological end proposed for this research, if the attempt is made to find out what are the various starting points of the diseased process from the normal. The first part of the investigation supplies, as has been said, an *apparatus physiologicus* wherewith to trace out and to estimate the extent of those abnormalities. The fringes of more or less normal gland substance, and the younger tumour nodules form a kind of intermediate territory, in which the traces of healthy action are not altogether hopelessly obscured. It is in dealing only with this kind of material that one can hope to indicate the exact point of departure of the disease. There is indeed an infinite variety of pathological appearances in the mammary structure; there is nothing of it, one may say, but is changed "into something rich and strange." But those vagaries of nature may be reduced to a few leading principles. In the first part of the investigation we profess to have established one or more important laws of the healthy mammary activity, and the whole of the pathological investigation that follows will be found to be nothing else than an illustration of the working of those laws under altered circumstances. It is proposed, therefore, to give in the first instance a number of illustrations of morbid physiological action within the breast, and to point out from time to time the relation of the same to the various kinds of tumours.

The first step in tumour formation: production of waste cells in the acini.

The most common appearance in the more or less healthy mamma adjoining tumours, and in certain parts of the tumours themselves, is an appearance resembling that of the early evolution of the mamma. The figure No. 21 is taken from the mamma near a tumour. It is not at all

Fig. 21.



Lobule of a mamma near the resting state. Numerous large pigmented cells within the acini and in the interlobular fibrillar tissue; sections of three blood-vessels to the left of the lobule. Magnified 160 diameters.

different from the mamma in the early stage of evolution, but there was no reason to suppose in this or in any other of the cases that the animal was subject to the ordinary cause of the evolution of the mamma from the resting state, viz., pregnancy. The effect, however, is the same; the acini are obviously subject to a certain degree of activity, they contain a number of the large yellow cells in their cavity, and there is a considerable number of the same large yellow cells in passage through the loose fibrillar tissue outside. This appearance is constantly found as the commencement of disease, and the process so far is a diseased

process solely because the excitation to it is something other than the natural excitation to the evolution of the mamma. The gland is disturbed from its resting state and proceeds to follow, to a certain point at least, the ordinary course of evolution. But, if one may so speak, it has been started along its wonted evolutional track on a false pretence. The evolution is spurious, and the end of it, as will be seen, is disastrous. Strictly speaking, however, the process is not one of evolution; it is rather the absolute effect of a certain low degree of excitation upon a mamma in the resting state.

Spurious evolution.

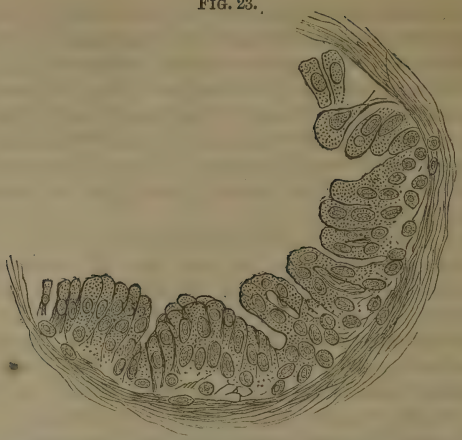
As we have already seen, the characteristic product of the lowest degree of excitation, whether at the end of involution or at the beginning of evolution, is the large granular pigmented cell. Now, in the involution, the excitation speedily comes to an end; the production of the large yellow cells is a passing phenomenon which the involution process gives few opportunities of observing well. In the evolution process it can be studied very much better; the cells are often found *in situ* within the acini, and large accumulations of them may be seen outside. But in the evolution also the phenomenon is transitory; the degree of the excitation is gradually increasing, and, for one reason or another, the large yellow cells cannot be easily seen in what we must consider to be the successive steps of their career. In the cases of spurious excitation, however, the circumstances admit of the mode of production of the yellow cells being much more deliberately observed. In the diseased process we realise partially that state of the secretion where it does not advance to the production of milk, but continues all the time to act at a uniform low degree. The characteristic yellow cell is here a much more stable product, and, as will appear, sometimes accumulates to form an epithelium of several layers. In certain cases the whole floor of an acinus has a yellowish tinge, a certain amount of pigmented substance being disposed round each nuclear cell. The acinus seen also in profile is found to have a complete circlet of yellow cells. Fig. 22 is a drawing of a portion of a lobulus of the mamma near a tumour. Several of the lobuli near it are at or about the usual resting state, and are about one fourth the size of the one figured, and separated from one another by the usual amount of fibrillar tissue. The whole of this pathological lobulus has a distinct yellow tint, and the yellow colour of the cells in the half acinus at the top of the figure is very well marked. Their substance is the ordinary granular pigmented substance, but their form is peculiar. It is neither the round form of the normal pigmented cell, nor the polyhedric form of the perfect epithelium; but it is more of the columnar or club shape. Most of the cells in the other acini of the

The waste cells of the pathological process are more stable than in the normal processes.

Fig. 22.

A pathological lobule. The uppermost acinus shows the pigmented cells as epithelium *in situ*. Magnified 160 diameters.

Fig. 23.



From the mamma of a bitch, adjoining a tumour. The epithelium massed in more than one layer, or in villus-like processes. *The granular substance of the cells is everywhere bright yellow.* Magnified 300 diameters.

Fig. 24.

From the mamma of a bitch, adjoining a tumour. Numerous villus-like processes of epithelial cells, growing from the recess of a duct. *The cells are all pigmented yellow.* Magnified 150 diameters.

lobule belong to a class that will fall to be described afterwards. Fig. 23 shows a somewhat similar shape of cell as in the upper acinus of Fig. 22. The preparation is taken from the very much affected gland tissue round a tumour, and the striking point of the appearance is the brilliant yellow of the entire semicircle of cells. Where the cells are lying single they are found to be more or less columnar; elsewhere they are fused together into villus-like processes, which consist of a double row of three or four columnar cells on end. A more remarkable degree of the same kind of aggregation *in situ* of the pigmented cells is seen in Fig. 24. This is taken from the tolerably healthy gland tissue near a tumour. The portion represented in the figure is evidently the recess of a duct, the epithelium of which has been, as it were, infected with the same kind of functional activity as may be seen elsewhere in the acini of the same case. All the substance that is made to appear granular in the woodcut is in the preparation of a bright yellow. The two perpendicular sides of the recess have a border of yellow granular substance, which can be seen clearly enough at some places to consist of large cubical cells. From the bottom of the recess there spring a cluster of papillary processes, some of which are cut obliquely and appear to be short, while two or three of them are long columns of uniform thickness, which are built up solely of large yellow granular cells arranged round a narrow central space. One of the columns of cells, it will be observed, bends over at the top.

The pigmentation of the cells implies a certain functional transformation.

In the class of appearances from which Figs. 23 and 24 are taken, there is evidently a great hyperplasia of the epithelium. But the whole essence of the pathological process lies in the fact that there is more than a mere hyperplasia or excessive reproduction of epithelium. The yellow granular appearance of the cells is certain evidence that they are subject at the same time to the functional activity of the gland. It has been argued at some length in Part I. that the formative activity of the mamma and the functional activity always go hand in hand. The formation of the secretion from successive sets of the epithelium presupposes constant relays of new cells, which, in the greatest activity of the function, are destroyed almost as fast as they are formed. What we have here is the formative excitation outrunning the functional. For whatever reason, the epithelial cells are not shed as soon as they undergo their degree of functional transformation, but they remain *in situ*. They do not form a many-layered epithelium after the ordinary pattern; they have rather a tendency to run out into a number of papillary processes. The reason of their accumulation *in situ* is probably, as has been already suggested, the fact that the excitation is not the progressive excitation of evolution, but a certain low degree of the functional activity called erroneously into play and acting at the same low rate for an indefinite time. The secretory product under these circumstances would appear to be a more stable product than are the waste cells produced by a corresponding functional stimulus in the healthy evolution, and no doubt the increment of the secretory force in the latter case accounts for the difference. The cell is, however, still a product of the secretion; its yellow colouring is conclusive on that point. It belongs to exactly the same category as the waste cells of the healthy process; and, to adopt the convenient formula often used already, those yellow cells are produced according to the law of endogenous cell formation. Such products, again, have been explained to be "metaplastic" or heteroplastic.

The large yellow cells as constituents of tumours.

The large yellow cells are not the most abundant constituents of the new growths in the bitch—in the human subject they are of exceptional occurrence—nor can any considerable part of the morbid structure be referred to transformations of them except in one or two cases; but they are found in almost all the tumours as an important concomitant of the

other processes, and they have a special importance for investigation from their striking colour. They are in fact, as we found also in the physiological part, to be taken as representing the waste products in general; and the explanation of pathological processes in the breast becomes much easier and more objective if they are used, with due caution, in this capacity. Up to this point we have found that, in the spurious excitation of disease, the pigmented cells are produced in excess within the acini. But in most cases it is not inside the acini, but in the fibrillar tissue outside that they are found in greatest numbers. In Fig. 14, illustrating the normal evolution, there is seen a large collection of precisely the same cells in the tissue surrounding the secreting structure, and it has been explained that the large accumulation at one point was in that case the result of an accident. Now in the mammæ subject to a diseased process, such collections are constantly found. The cells are frequently deposited in several rows between the acini—which are themselves the seat of morbid changes to be described afterwards—but the largest collections of them are in the wide tracts of fibrillar tissue which separate the lobuli in the resting state, and which become much more extensive in the mammæ of aged animals, and in women at or beyoud the climacteric period. In those tracts of fibrillar tissue the pigmented waste cells are sometimes found in large irregular heaps; more frequently they are seen to be arranged in certain regular lines, which obviously correspond to the pre-existing lymphatic spaces. In such situations they usually lose their roundness; they become oblong, with their opposed ends flattened, and not unfrequently they become long, narrow, and fusiform. The nucleus, which is generally visible, takes on a corresponding alteration of shape. Fig. 25 is a high-power drawing of one small portion of a field that is quite covered with the large round yellow cells. It is from the diseased mamma of a bitch, the same from which Fig. 22 is taken; the latter, from the less changed part of the gland, will serve to show pictorially where the yellow cells in the fibrillar tissue have come from. The pigmented cells of Fig. 25, which are disposed in groups in the fibrillar tissue and which contribute to the bulk of the tumour, are the same yellow cells that are seen *in situ* in the acini of the gland. If the extra-acinous collection is examined closely, it will be seen to be made up of rows of cells which unite to form alveolar groups. Often a single file of cells extends for a long distance across the field; or there may be a double row, or any variety of grouping up to the alveolar collection, half a dozen cells or more in breadth at its broadest part. In the immediate neighbourhood of acini, or in the spaces between them, the arrangement of the yellow cells nearly always follows the circular outline of the acinus. It does not appear

Fig. 25.

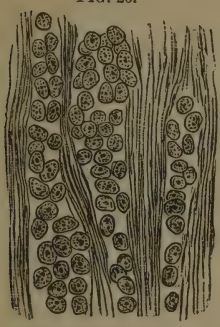
From a mammary tumour in the bitch. The fibrillar tissue of the mamma invaded by rows and alveolar groups of *large yellow granular cells*. Magnified 300 diameters.

that the large granular pigmented cells ever undergo division of their substance. If the collections of them increase, it is by the addition of fresh supplies from the original source. But they are found to undergo certain transformations, and the derivatives of the pigmented cell, the cells resulting from such transformation, appear to multiply in the usual manner. The transformation consists most commonly in the loss of their pigmented cell substance.

The grouping of the pigmented waste cells illustrates the formation of skirrhus cancers.

In order to take advantage of the illustrations of extra-acinous grouping of cells, which are afforded by the waste cells of the pigmented stage, it is desirable to refer here to a very common type of tumour of the human female breast, although its component cells belong to another class of waste epithelial products. Fig. 26 is a drawing of one of the most common appearances in the intensely hard skirrhus of the breast of women at or beyond the climacteric period. In this particular case the patient was 58 years old. If the figure is compared with Fig. 25, the cells will be found to be very different; they are rather less than half the size, they are little else than nuclei without cell substance, and they have no pigmentation. Those differences are, however, unessential to the argument; they are merely the differences between one kind of epithelial waste product and another. The essential point of similarity is the presence of cells in the interfascicular spaces, and the grouping of the same. The position of the cells in the two cases is precisely alike. A certain number of them are arranged in single file, and these have frequently a cubical or disc shape from the flattening of their opposed sides; the greater number of them are grouped in alveoli of varying breadth, and those alveoli are obviously made up by the fusion of two or more rows of cells. In short, if the preparations from the case of skirrhus of the human breast are compared with the preparations from many cases of tumours in the bitch, which have the pigmented cells as part of their constituents, the resemblance in the grouping of the cells is found to correspond throughout; and there arises the strongest presumption that the cells of the skirrhus are of the same origin and subject to the same influences as the pigmented cells, which are known beyond all doubt to be the waste products of a feeble degree of the secretory activity. The strong presumption that arises at this stage of the inquiry will be confirmed by further evidence at a later stage. In the meantime it is necessary to observe that the cells of skirrhus, although they are in great part situated outside the secreting structures of the gland, or the remnants of the same, are not all so situated; and further, that it is precisely in those breasts that have an enormous development of the interlobular fibrillar tissue, that is to say, in the breasts of women at or beyond the climacteric period, that the skirrhus form of tumour usually occurs.

Fig. 26.



From a skirrhous tumour of the human female breast. The fibrillar tissue of the breast occupied by rows and alveolar groups of nuclear cells. Magnified 300 diameters.

Criticism of Virchow's theory of skirrhus of the breast.

The appearance drawn in Fig. 26 is selected, because it is almost exactly the same as that figured by Virchow to prove the origin of the cells in cancer of the breast from the pre-existing connective tissue cells of the part.* The direct evidence in favour of Virchow's theory is

* *Cellular Pathologie*, p. 539, Fig. 146. See also the diagrams in Virchow's *Lectures on Tumours*, Lecture V.

necessarily of a defective kind; it is next to impossible to prove that or any other theory of cellular growth by direct and objective demonstration. But Virchow's theory of the origin of the cells of cancer is only a corollary of one of the doctrines of the cellular pathology. Instead of the universal exudation or plastic lymph of the earlier school of pathologists, he finds that the all-pervading connective tissue, the cellular elements of which he himself demonstrated, is the matrix tissue of new growths.* Virchow's substitution of the cellular elements of the connective tissue for the formative blastema or plastic lymph of his predecessors is now an accepted doctrine; but it will doubtless be remarked by many that Virchow has borrowed an error from the doctrine which he superseded, when he attributed the same universality to his new matrix tissue. In this respect he has merely shifted the centre of a position that is from first to last erroneous. Many important additions that have been made to pathological knowledge since Virchow published his theory have helped to break down this closed circle, this exclusive prerogative of the connective tissue elements, and it will probably appear to a later generation that one at least of Virchow's memorable and inspiring "Einheitsbestrebungen" was a striving after unity where in nature there is only diversity. But its place in the connective tissue theory is only a part of the *primâ facie* argument in favour of Virchow's doctrine of cancer. A more powerful argument, inasmuch as it explains a more obstinate fact, is the satisfactory reason that the theory supplies for the heterology of the cancerous growth. If the cancer cells were of epithelial origin, Virchow argues, the growth which they build up would be a mere hyperplasia; there would be nothing to account for the obvious difference in type between the cells of the cancerous tumour and the epithelial cells of the part. The atypical element or the element of heterology, in Virchow's theory, is supplied by deriving the quasi-epithelium of the new growth from cells not of the epithelial category, that is to say, from the connective tissue cells. There is supposed to be an "epithelial infection" of the connective tissue cells, whereby they produce elements unlike to themselves and resembling epithelium. This is, no doubt, a mode of generation of the tumour cells which meets the circumstances of the case, while the production of cells by ordinary generation fails to do so. But any such elaborate hypothesis is wholly superfluous. In the first part of this research it has been shown that there are large numbers of cells produced from the epithelium of the mamma which, from their mode of origin, are metaplastic or heterologous. All the waste products of the secretion are in fact metaplastic, and it is these same waste products, and still more subtle gradations of them, that we meet with, under altered circumstances, as entering into the formation of tumours.

The theories of Köster and Classen.

The account here given of the origin of the cells of skirrhus has an obvious relation to the theories of Köster on the one hand and of Classen on the other. According to Köster,† who investigated chiefly epithelioma of the skin, the cells of the new growth lay in the lymphatic channels and were produced *in loco* by germination of the endothelium. According to Classen,‡ who based his conclusions chiefly on a case of tumour of the cornea, the elements of the new growth were cells that had wandered into the tissue by the lymphatic channels, and which were in fact the colourless corpuscles that had escaped from the blood vessels.

Returning to the illustrations of morbid physiological action within

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* *Cellular Pathologie*, p. 485.
† *Die Entwickelung der Carcinome und Sarkome.*
‡ *Virchow's Archiv*, vol. 50.

the secreting structure of the breast, and taking the phenomena in convenient order, we come next to a certain class of pathological processes which play a far greater part in the formation of new growths than those last described. These also have their type in a certain phase of the normal activity of the breast. They correspond to a more advanced stage of evolution, or, absolutely, to a higher degree of functional excitation. In the description of the evolution process in the cat, the stage of evolution succeeding the earliest or pigment-cell stage was found to have less intelligible features than the stage that preceded it or than the stage of mucus-production that came after it. Yet the same appearances, however difficult of interpretation, occurred uniformly in the animals at the same stage of pregnancy, and corresponded to a 3 or 4 inch size of fœtus. The condition is that figured on page 147, and with a lower power, on page 148. The cells are arranged within the acini in somewhat regular order, forming a circlet round the margin in the profile view, and being strewn over the floor at narrow and regular intervals in the infundibular view. At the same time, the acini were generally found to contain a peculiar granular material, which in some cases amounted to an actual fluid of high refracting power. Now, in a good infundibular view of an acinus, the peculiar granular material which in other acini filled up the free cavity, appeared to be disposed round each of the nuclear cells strewn over the floor. It is true that it is never seen in that situation in great amount; the cells at that stage of evolution are roughly speaking naked nuclei of considerable size. But it is difficult to imagine where else the granular material of the secretion comes from, if not from a transformation of the very unstable cell substance of the acinous cells, or to imagine what is the secretory activity of those cells unless it be to assume a certain protoplasmic investment and afterwards to give it up as secretion. These are steps however that do not in health ever come under actual observation. But there is the analogy of the earlier and later stages of evolution to fall back upon for an explanation. In the earlier stage, the nuclear resting cells acquire a large investment of pigmented cell substance, which, however, they do not again give up as secretion within the acinus. They are thrown off from the acinus entire, and the stripping of their cell substance which did not take place in the proper habitat of the secretion, is actually seen to be accomplished in some cases in the tissues outside, and, in any case, in the special depuratory apparatus of the lymphatic gland. Again, actual vacuolation of the large yellow cells in their position outside the acini is to be seen in the preparation figured on page 146. Now, it is to be held as a mark of increased functional excitation when the secretory act, such as it is, is performed inside the acinus. But there is none the less an accompanying cellular waste. There is no small amount of cellular waste in the stage of mucus production, although the waste cells are either small round nuclei or the peripheral masses of vacuolated cells that may be infinitesimally small; and even in the stages of the function that are little short of perfect, there are the colostrum cells which are a form of cellular waste. The kind of waste cell that is characteristic of the stage of evolution or of the degree of excitation that we are now reconsidering in view of its applications to pathological processes, is a large nuclear cell. The figure on page 148, from a mamma in the middle period of normal evolution, is taken as showing those waste cells in their passage through the interlobular tissue, after the analogy of the large yellow cells in transit or of the small round nuclei of the mucus stage crowding the tissues around the acini and lobules. This, then, is the type of waste cell that reappears under altered circumstances in the important

Review of the second stage of normal evolution.

The waste cell of the second stage of evolution is the type of most of the cells in cancer of the human female mamma.

pathological processes that have now to be described. The large nuclear cell of somewhat variable shape, with little or no cell substance, and with one or more nucleoli, is by far the most common cellular element of both the hard and soft cancers of the human female breast, while in the tumours of the dog and cat it occurs frequently and under such circumstances as leave no doubt as to its origin. In the evolution of the breast in pregnancy this waste cell corresponds to a passing phase of the process; in the diseased processes of the breast it represents the effect of a certain imperfect degree of the functional excitation acting at the same low rate for an indefinite time.

The pathological process generally attacks the mamma when it is in the resting state.

It does not appear, however, at least in the case of animals, that the degree of excitation whereby that particular waste cell is produced can be reached, even in disease, without the earlier and lower degree of excitation, the first departure from the resting state, having preceded it. Either in the fringes of more or less normal mamma, or in parts of the new growth itself, the earlier process is nearly always present, and there are also clear gradations to be found from the one to the other. Generally speaking, the largest and apparently unaffected part of the chain of glands shows only the earlier process, characterised by the formation of the large granular pigment cells; the particular portions of the chain where the tumours occur are those parts of the gland in which the morbid excitation has begun earlier, or has progressed more rapidly, or has in general met with more favourable conditions. But although the facts themselves, as derived from the material of this research, go to show that, in dogs, the diseased excitation attacks the gland as a rule in the resting state, and leads it so far through a course of spurious evolution, it is not to be forgotten that there may be disastrous interferences with the activity of the gland at other times, or under other circumstances. We shall have occasion to notice what is the special pathological effect of an interference with or disturbance of the functional excitation when the secretion is at the height of its intensity. The result in that case is not, as far as is known, tumour formation, but inflammation and the formation of an abscess. The remaining conditions of the mamma are the process of involution, and the slow process of evolution. It is possible to imagine the involution to be arrested before the gland had been brought safely to the resting state, and the enfeebled excitation to go on for an indefinite time at the point where the progress of involution was checked. The result in that case would, according to our knowledge of the process and its possibilities, be no doubt a collection of heteroplastic cells forming a tumour. Again, as regards the prolonged evolution process, it is not difficult to imagine circumstances wherein a part at least of the gland may leave the beaten track of health. The death of the fœtus must be held to be a possible source of irregular cellular production within the mamma. All such possibilities are not to be left out of sight; but, so far as the present facts go, it is from the resting state that the gland is disturbed by some unknown stimulus, and the diseased process that is set up follows the physiological law of evolution. We have already had under notice certain illustrations of the pathological processes that have their type in the earliest stage of evolution, and with the observation that those processes are, generally speaking, the earliest phase of the disease in all cases, we now proceed to consider the characteristic pathological processes which are due to an increased degree of the glandular excitation, and which are a much more important element in the formation of tumours.

Fig. 27 is a drawing of one of several contiguous acini from the diseased mamma of the bitch. One side of the acinus, seen in profile, has the epithelium massed either in more layers than one, or in a

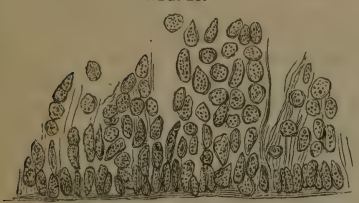
number of knob-like processes. The appearance is perfectly characteristic, not only of the whole of that particular case, but also of several other cases; and the process, with its modifications and developments, is one of the most common of the pathological processes within the breast that make up, in the gross, a cancerous tumour. Several other cases of tumour in the bitch, both the cases in the cat, and certain cases in the human subject are directly referable to the same initial process. The acini are for the most part greatly enlarged, so much so in certain cases that the section of the tumour has to the naked eye a reticular appearance depending on their prominent outlines. In those of them where the process is not complicated, the wall of the acinus, or the floor of it, is seen to be covered with a number of wart-like prominences; as many as 10 or 12 of these have been counted strewn over the floor of a single acinus. The prominences are for the most part simple aggregates of nuclear cells having a distinct nucleolus, and built up with some regularity so as to leave a small central lumen. But the earlier stage of these prominences is easily seen to be a narrow solid column of cells; and those small piles of cells, again, are simply a modification of the many-layered condition of the lining cells of the acinus.* Fig. 28 is a drawing of a part of

Pathological processes corresponding to the second stage of normal evolution.

Fig. 27.

From a mammary tumour in the bitch. The epithelium of the acinus massed in several layers or in processes. Nuclear condition of the cells. Magnified 300 diameters.

Fig. 28.



From a tumour of the human female breast. Portion of the wall of an enlarged acinus, showing the epithelium massed in several layers. Nuclear condition of the cells. Magnified 300 diameters.

* As an opportunity will not be found to return to the point, one of the common developments of the intra-acinous papillary processes may be referred to in a note. The lumen that tends to form in the centre of the column of cells is often occupied by a vessel or vessels. The papillary process then acquires a sort of bi-pennate appearance, the line of the blood vessels forming the raphe, and the epithelium being arranged regularly along each side of it. The vascularised processes often anastomose, in the way that will be afterwards described for the trabecular structures within the acini, and there results a network of columns having an epithelial covering on each side, the original outlines of the acini being in the end obscured. When the vascularised papillary processes do not anastomose, they project into the acini as if they were imperfect septa. Langhans (*Virchow's Archiv*, vol. 58) has described the same appearance, but he attributes it to an actual breaking down of the septum between two acini, as in emphysema of the lung.

App. No. 4.

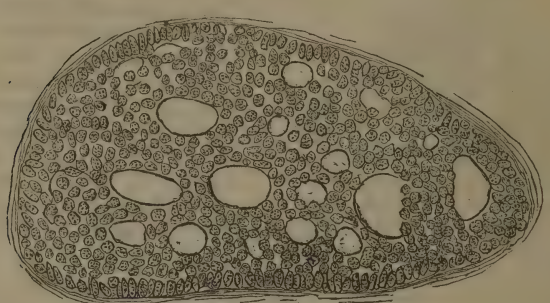
On the Ætiology of Cancer, by Dr. Creighton.

one side of an acinus from a female human breast subject to cancerous disease. The entire tumour, which was situated at one side of the nipple, of small extent, well circumscribed and of somewhat soft consistence, was made up of nothing else but this condition of the acini and of the further developments and direct modifications of the same. The tumour is in fact representative of the intra-acinous class of new growths, and these correspond most closely to the clinical division of medullary cancers of the breast. The skirrhous tumours of the breast, on the other hand, are chiefly extra-acinous. The figure shows an appearance very much like that of an epithelium of many layers. The lowest layer appears of a deeper colour, being made up of the more cylindrical and pyramidal forms of cells closely packed together; and that is precisely the character of the lowest layer of a normal epithelium of several layers, as, for example, that of the trachea. The upper cells are rounder and separated by a larger amount of intercellular substance, and the free border may be seen to run out into processes of the same kind as those referred to in the preceding figure. Now, all the cells that line the walls of these acini, and in some cases occupy the entire space of the acinus, are of the nuclear kind. The full significance of this fact will be made clear by means of contrast with another case to be introduced shortly.

It has been pointed out that the columnar processes of the large yellow cells, such as are figured on p. 178, showed a tendency to bend over at their free end. The same may be observed in Fig. 27. The round disc-like appearance in the upper of the two processes, is evidently the transverse section of the process that has doubled upon itself and is now proceeding at right angles to its original direction. This is very commonly observed; and still more commonly one finds that the space of the acinus is occupied in all directions by trabecular columns of cells, which are nothing else than the processes that have become fused together at their free extremities. Fig. 29 is a drawing of an acinus

Filling up of the acini by trabeculæ of nuclear cells.

Fig. 29.

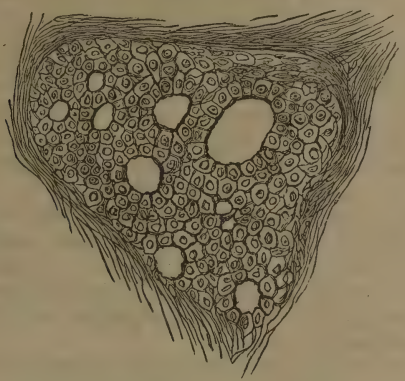


From the same case as Fig. 28. An acinus filled with trabecular processes of nuclear cells. Magnified 150 diameters.

from the same case of tumour of the female human breast as Fig. 28 has been taken from. The entire space of the acinus, it will be observed, is occupied by anastomosing columns or trabeculæ of cells; the cells are all of the same nuclear kind, with a certain amount of intercellular substance, as has been already described for Fig. 28 of the same case. Now, the subjoined figure No. 30 has a great resemblance to the preceding, but it shows differences in the character of the component cells which are of the highest importance. Fig. 30 is from a tumour of the

human male breast.* The patient, a man past middle age, had a tumour in each breast, one of them quite small and firm, the other larger and in parts softened. The drawing is taken from a firm and undegenerated part, and is strictly representative of the general condition. The

Fig. 30.



From a tumour of the human male breast. An acinus filled with trabecular processes of polyhedric nucleated epithelium. Magnified 150 diameters.

growth consisted of greatly enlarged acini, sometimes packed closely together, but in general with a certain amount of coarse fibrous or adenoid-like tissue between them. Within the acini, the epithelium was of an exquisite polyhedric type, nucleated cells with a broad fringe of almost homogeneous protoplasm. There was everywhere a considerable hyperplasia of the epithelial cells, which sometimes gave the floor of an acinus a ridged appearance, but more often resulted in the trabecular filling up of the free space of the acinus, as shown in the figure. The perfect polyhedric shape of the epithelium was not everywhere present; in some situations the cells were more elongated or lozenge-shaped, but there was everywhere the same relation between the central nucleus and the investing cell substance. When the cells were seen edgewise they appeared to be excessively thin plates, resembling endothelium. The only other point that requires to be mentioned by way of description is, that the softening or degeneration of one of the tumours consisted in the caseation of large numbers of the epithelial cells within the acini. The appearance of the softened parts to the naked eye was caseous, and with the microscope the acini were seen to be filled with heaps of rounded cells which had the usual blurred outlines and opaque substance of cells that had become caseous.

Contrast between the acinous cells of tumours of the male and female breasts.

The whole significance of the special points of this case lies in the fact that it was a tumour of the male breast. The male breast, long before the individual has reached maturity, has lost by disuse the capacity of functional excitation with which it was originally endowed; the channels by which the functional stimulus would pass to the gland have presumably been stopped up. The functional aspect of its life has been completely obliterated, while the structural framework of the gland remains in some form or other, which is not well understood. Now the latter is still capable of excitation; it may be subject to irritant influences like any other part of the body. In the present case the patient was a blacksmith, whose work exposed him to certain kinds of pressure or concussion on the upper part of the thorax. The effect of the excitation,

The significance of the form of epithelium in the cancer of the male.

* The patient was at St. Thomas's Hospital under the care of Mr. Wagstaffe, who has reported the case in the *Medical Times and Gazette* for Aug. 1st, 1874.

in whatever way the latter operated, is seen to be a purely hyperplastic effect. The new growth of epithelium is perfect epithelium, and not the waste products of a feeble secretory stimulus. Again, the transformation of this epithelium is not any of the transformations of secreting epithelium, for instance into a mucous or a fatty substance, but it is a *caseous transformation*. Caseous transformation of hyperplastic epithelium occurs elsewhere in the body, very commonly in the epithelium of the lung alveoli and in the cells of the suprarenal body,* and it cannot escape notice that the cells in both of those situations are epithelial cells in exactly the same position as the epithelial cells of the male breast; that is to say, they agree in being not subject to the ordinary functional excitations of epithelium, and they have a considerable morphological resemblance. The acinous cells of the male breast and the cells of the suprarenal body are both of them the epithelium of a rudimentary or discarded secretory organ, and the lining cells of the lung alveoli are so unlike secreting epithelial cells that they have been sometimes described, not without good reason, as an endothelium. It will, in short, probably turn out to be a sound generalisation, that the caseous transformation of hyperplastic epithelium befalls only those epithelial cells which are subject to no secretory excitation.

The more or less nuclear form of cells in the tumours of the female is due to a degree of the functional excitation.

To return to the comparison of the two figures No. 29 and No. 30. In the latter, the hyperplastic process can be seen by itself; if it is succeeded by another process in the individual cells, the latter is a process of caseous degeneration. But in the diseased acinus of the female breast, the hyperplastic or formative process and the functional or transforming process are both implicitly present in one and the same act, and that is the reason why the cells are always seen in the nuclear state. The question may reasonably occur here, as it may have occurred before in the course of this exposition, What end is served by insisting upon those apparently trifling and, as it were, metaphysical differences between one kind of cell and another? The answer is that the malignancy of epithelial tumour cells appears to depend greatly on those differences in the form of the cells and on the circumstances under which they occur. Every new epithelial cell that is formed in the secreting gland is destined to be transformed. The multiplication of cells within a secreting gland can never be a process of growth alone, neither in health nor in disease; and if, in disease, the formative process outruns the functional and leads to a heaping up of the cells in papillary processes or in more layers than one, those cells are still not exempt from a functional excitation. From the circumstances of the case every cell within the mammary acini is made subject to the law of the secretion, which is the unhappily named law of endogenous cell for-

* The statements as to the suprarenal body are not without some basis of observation. The writer has in his possession a large hyperplastic tumour of the suprarenal body, which was caseous at certain parts. The non-caseous parts of the tumour were made up of cylinders of cells resembling the epithelial-like cells of the normal organ, and the cells of the caseous portions differed from the others only in their somewhat indefinite outlines and opaque substance. In this case there were secondary tumours in the liver and lung, which had the same (suprarenal) structure as the primary tumour. It may be mentioned also that, in the case of tumours of the male breast, the axillary lymphatic glands were found to be affected with the disease some time after the mammary tumours had been removed. Where the element of malignancy lay in these cases is not quite clear but this difficulty need not invalidate the argument that is pursued above. (Since the above was written, an examination has been made of one of the axillary lymphatic glands, removed by operation. The gland was no doubt secondarily infected, and it showed the same trabecular kind of new growth as the primary tumour. But it is a very remarkable circumstance that the cells composing the trabeculæ belonged, not to the class of nucleated polyhedric epithelium, as in the primary tumour, but to the nuclear class of cells with which they are contrasted in the text.)

mation. The transformation of the secreting cell is, as we have seen in Part I., always referable to that law of cellular activity. The cell may be transformed entirely into a vacuole full of fluid, or it may be transformed into a vacuole and a cell, or it may remain simply a transformed cell; but the act of transformation is always present in one degree or another and the "metaplasia" is inherent in the cell, however little it may seem to show it. Those degrees of the vacuolation or endogenous process have already been represented as a series, the middle terms of which were most intelligible, but both of whose extremes had also an existence in fact. The complete transformation of the secreting cell into milk drops is the one extreme, and at or near the other end of the series comes the particular nuclear cell whose pathological properties are now under consideration. It may be diagrammatically supposed to result from the gradual encroachment of the peripheral mass on the vacuole, till the latter is entirely obliterated. From another and more objective point of view, it is the product of a low degree of the secretory activity. It is necessarily a waste product, and in those normal processes where it occurs it is safely disposed of; but where it is due to the spurious excitation of disease, it remains at or near the place of its origin. There, it is not only an encumbrance and a superfluity, but moreover an outcast and an alien, out of harmony with everything around it, and ready to become in its turn the centre of a vigorous and hostile organisation. *The "parasitism" of the tumour is the literal parasitism of its component cells.* The point in this morbid process that is essential to the formation of a tumour is what has been already named the more stable property of the waste products. Instead of being discharged from the gland as soon as formed they remain and multiply in their place of origin. The process of division may be observed in some of the cells of the lowest layer in Fig. 28. The cell becomes elongated, a nucleolus appears at each end, and a line of division appears in the middle. Now the tardiness which allows the waste cells to be massed in the acini and to multiply there, is to be explained by an argument that has been used already. The spurious excitation of the gland is not so much a phase of evolution as a certain low degree of the glandular force which acts with the same intensity for an indefinite time. It wants the increment of the evolutional force, and that difference probably accounts for the greater stability of its products. It is not to be forgotten however that the spurious evolutional excitation, which in all cases seems to pass through the initial stage characterised by the production of large granular pigmented cells, may proceed also in some cases to act at a point of intensity beyond that which has been last discussed. And with this remark we come to consider another group of pathological processes and other varieties of tumours.

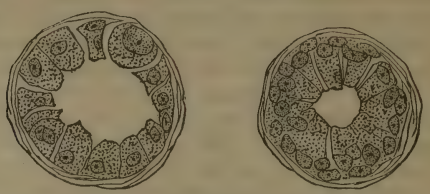
The "parasitism" of a tumour.

However far the false stimulation of disease may carry the mamma from the resting state towards its perfect evolution and its perfect secretory activity, the stages of the diseased process are always more tardy than in the evolution of pregnancy, and the pathological investigation often affords an opportunity of detecting some particular state of the mammary epithelium, which in the normal study was rather a matter of logical proof than of actual observation. Thus, in a diseased mamma the complete set of cells within an acinus may be observed to have the pigmented granular condition, while in the evolution of health seldom more than two or three pigmented cells are seen *in situ*, although they may be abundant enough outside the secreting structures. The well marked stage of mucus production that occurs in the latter half of evolution may be also more deliberately observed in the spurious exci-

The pathological processes amplify the details of the physiological.

tation of disease. The gland or some part of it becomes for the time being a mucous gland. Fig. 31 shows a pair of mammary acini which

Fig. 31.



Mammary acini, from two different pathological cases in the bitch. The epithelium in the form of perfect mucus-producing columnar cells. Magnified 300 diameters.

are taken from two different cases in the bitch. It would be difficult to obtain from any part of the digestive tract more perfect examples of mucus-producing structures. In the healthy mamma, although there is abundant evidence that a certain incomplete degree of the functional excitation both in involution and in evolution has for its effect the production of mucus from the secreting cells, those cells are not to be found ever at that point of their existence when they have the characters of perfect untransformed mucous cells. These characters are a somewhat columnar shape, a nucleus placed towards the attached border of the cell, and a large amount of cell substance which has the peculiar and, as it were, succulent aspect found in the secreting cells belonging to that class. In the corresponding stage of the evolution of pregnancy, the cells are found to be all of them vacuolated more or less extensively, as in Fig. 17 ; the condition of the gland is exactly analogous to those states of the intestinal mucous membrane or parts of it where the epithelial cells are found in the condition of goblet cells. Why the production of mucus from the epithelium of the mamma should coincide with a subsiding or an incomplete degree of its functional force is not at all clear. The question of superiority as between the fatty secretion of milk and the albuminoid secretions of the digestive tract would appear to be a question as to the greater specialisation of the former. However this may be, the mucous transformation of the mammary cells occurs at exactly corresponding periods in the parallel processes of involution and evolution, and it may be taken absolutely to be the characteristic effect of a limited functional excitation.* Corresponding to this degree of the secretory force there is a group of pathological processes in the mamma which are of

* An interesting observation is recorded in a case from the clinique of Professor Friedreich at Heidelberg (Report by Dr. F. Schultze, in the *Berliner klinische Wochenschrift*, No. 42, 1874). The patient, a married woman aged 26, was admitted suffering from constant pain in both breasts and a scanty discharge of colostrum-like milk. She had borne one child $2\frac{1}{2}$ years before the commencement of the symptoms, and had lived apart from her husband for the last two of these. She had suckled the child regularly for 6 weeks after its birth; but after that interval the supply of milk was suddenly checked, and the cause of the stoppage seemed to be psychical disturbance (domestic troubles). No milk abscess formed, and there were no symptoms of any kind in the breast for $2\frac{1}{2}$ years, when the mastodynia with colostrum secretion began suddenly, first in the right breast, and in the left three or four days after. It had existed for 7 months before her admission, and she was under observation for 9 months longer, during which time there was little or no change in the symptoms. The report of the case contains several points of interest, but only one of these concerns us here. During each menstrual period, the breasts became more turgid and more painful, and the secretion, of which a few drops could always be expressed, was not the milky fluid found at other times, but a clearer and more serous fluid, which also contained nucleated colostrum cells, but a much smaller proportion of milk globules.

frequent occurrence, and which are the point of departure for many of the tumours in the bitch and for some of the varieties of mammary cancer in the human subject. Those tumours often correspond closely to the cystic sarcomas, or myxomas, or colloid cancers; but as we have been led, for sufficient reasons, to avoid treating the tumours according to their classes, or in their ontological bearings, the names are mentioned here solely to show what are the familiar tumours that we now come, in the course of this aetiological research, to deal with.

Pathological processes corresponding to the physiological stage of mucus-production in the mamma.

The mucus gland structure of Fig. 31, which, although perfect of its kind, is itself phenomenal in the mamma, is found more commonly in certain states of transformation. Enlarged acini are found in which the cells, forming a circlet round the wall, are spherical and distended with mucus-like protoplasm, or actually vacuolated like the cells in Fig. 8 on page 132. The cavities of acini are not unfrequently seen to be filled with the same large vacuolated cells. The distinction between these and the colostrum cells proper is in their substance only; the form is the same, but the substance in the one takes on the degree of staining characteristic of mucus or of mucus-yielding protoplasm, while in the other it remains mostly unstained and of a greyish appearance. In two of the cases in the bitch, another variety of transformation is observed. The acini are filled with large collections of mucus penetrated with vesicles in all directions, and in this mucus lie a number of round deeply coloured nuclei. In favourable specimens the vesiculated mass of mucus is seen to be an aggregate of many vacuolated cells which have the round nuclei in their cavity or on their periphery. As to the cells that line the wall of the acini in those cases, they are also nothing but deeply stained round nuclei, with no obvious cell substance. Two cases of tumour in the bitch, one of which had a superficial cyst and was highly malignant (the liver being full of secondary tumours) were made up chiefly of groups of acini containing cells of the above category. Generally speaking, the acini were grouped in the ordinary lobular arrangement; so far, the change in the gland occurred uniformly throughout its substance. The interlobular tissue was extensive, juicy, and often filled with numbers of the large yellow and other cells. Inside the acini the cells were either in more layers than one, or they ran out into processes, or they completely filled up the acinous space. In these points the pathological process resembled that already described for two other varieties of waste products, the large yellow cells and the kind of cells in Fig. 27 and Fig. 28. The difference lies in the fact that the cells now under notice are smaller and rounder or more perfectly nuclear. Where the vacuolation process is obvious, they are the correlated cellular product of a more complete vacuolation. Whether the vacuolation is obvious or not, they correspond to the waste cells where the functional excitation is considerable, and they have the closest resemblance to those drawn in Fig. 9, and in Figs. 5 and 6. The normal mamma (of involution) from which the two last are taken shows other cellular products of vacuolation besides the small round cells. These are the crescentic, or rhombic, or triangular, or rod-shaped cellular bodies which are derived from the vacuolation of cells in a perfectly intelligible manner. Now, the same variety of shapes is found among the cells within the acini in the pathological states of the mamma that correspond to the mucus-producing period. In particular the greater part of the tumour in one of the cases in the bitch (other than one of the two just mentioned) consists of alveolar groups of those cells, and the alveolar arrangement is clearly enough seen to be the earlier acinous arrangement. The cells, while retaining their various shapes, have very generally a narrow fringe of homogeneous protoplasm, besides

Account of a special case in the bitch.

the deeply coloured nucleus. This tumour would be considered a myxoma.

There is, however, among the cases collected, one in particular which illustrates so many of the pathological processes at once that it may be selected for a more detailed and circumstantial description. The animal was an old setter bitch. In July 1873, a tumour was removed from one part of the mammary chain, globular in shape and lobulated, about two inches in diameter, firm in consistence and yielding on section a clear yellowish or brownish juice. There was one very small point of cartilaginous tissue near its centre. This tumour belonged to a variety that will fall to be described afterwards, among the concluding illustrations of pathological processes. After the removal of the tumour, the dog was worked during the two following shooting seasons. In June 1875 it was brought back for treatment, the disease having re-appeared. There was now a large soft tumour towards the inguinal end of the other mammary chain, and there were several smaller nodules throughout the whole length of the mammæ on both sides, besides a more diffused enlargement in the lower thoracic part of one chain. The animal was considered to be past surgical treatment and was killed. The liver contained a number of small rudimentary nodules, and in the mediastinum there was an enormous lobulated mass of medullary consistence. At a point in the vena cava inferior about two inches below its termination in the auricle there was an oval mass of the same consistence, rather smaller than a hen's egg. It was adherent within the vein anteriorly by several roots or processes, but there was a slit-like passage between it and the posterior wall. The vein was seen *in situ* to have a fusiform distension corresponding to the tumour within it; it gave off one or two small branches opposite the middle of the tumour, and at the lower and broad end of the tumour it broke up into three branches about a quarter of an inch wide. One of these, which was perhaps the chief trunk of the vein, appeared to be continuous with the capsule of the large medullary mass in the mediastinum; the tumour in the upper part of the vena cava seemed, therefore, to be an extension upwards of the latter. There was no marked change in the thickness or capacity of the right auricle, but the muscular layer of the vena cava at its termination in the auricle extended downwards for about two inches, and was of great thickness. The new growth in the mediastinum and within the vein had the same structure as the principal mammary tumour, and is to be viewed as secondary to it, from whatever matrix tissue it may have proceeded.

Various conditions found in the mamma in this case.

Some of the small mammary nodules were cartilaginous; others did not differ in gross characters from the gland tissue that surrounded them except in being circumscribed and of greater density or closeness of texture. The diffused enlargement, again, which extended over 2–3 inches of the mammary chain, obviously owed its special character to some process going on more or less uniformly throughout the gland over that area. To take advantage of the evident richness of this material, several sets of sections were made from different portions of it. Many parts of the mammary chain of glands were found to show the perfectly typical resting state, as given in Fig. 3 on page 129, taken from a mamma at the end of the normal involution. Another common appearance was that of the acini of the first evolution stage, with large yellow cells within and around them. Some of the smaller nodules were made up in part of large collections of the pigmented cells in the fibrillar tissue. Sometimes an entire lobulus is encountered the acini of which have the mosaic of perfect epithelium as in the fully developed gland. The epithelial cells, however, have unusually large and oblong nuclei, as shown in the right-hand group of cells in Fig. 2 drawn from

another case. But the processes most characteristic of the case belong to the stage of mucus production. One of the acini of Fig. 30, showing perfect mucus cells, is taken from this case. Other acini, again, have a circlet of spherical mucus cells, or the same vacuolated; and there are to be seen in reality those gradations in tint between the distended spherical mucus cells and the large yellow cells of an earlier stage, which in the study of the physiological evolution are rather an inference than a matter of observation.

But the most instructive appearance of cells within the acini is that drawn in Fig. 32. The figure contains two adjoining acini, the upper

Fig. 32.

Mammary acini of the bitch (pathological). The epithelium massed in several layers. The cells columnar and nucleated, or spindle-shaped. Magnified 300 diameters.

of which is incomplete, but shows very well the cells individually. The lower is a complete acinus with two apparent diverticula, which are no doubt the infundibula of adjacent acini that have been included in the same place of section. The acinus, it will be seen, has a small free space in the centre, and several layers of cells on its wall. This is the same pathological process that we have had to consider before, and as in the former cases, except in that of the male breast, the many layered epithelium implies more than a mere hyperplasia. In the cancer of the male breast the cells were perfect epithelial cells, but in the other cases of hyperplastic acini, as in this, the cells are of another type. In Fig. 28, from a soft cancer of the female breast, the lowest layers are oblong nuclear cells, while the upper cells are rounder. In the present case, the cells next the wall are oblong or spindle-shaped, and the marginal row are rounder. In both cases the form of the cells is owing to the fact that there is not merely a hyperplastic process going on, but a functional process as well; there is in fact the dual activity of the secreting gland. In the present case, the activity corresponds to that degree of excitation which produces mucus from the epithelium. One acinus from this case has been figured already in which the epithelium has the perfect mucous type, and the same kind of cylindrical cell with the nucleus at its base may be seen in the half acinus at the top of Fig. 32. The obvious and unmistakeable secretory change in the cell is where it becomes

Spindle-shaped cells in the position of epithelium.

globular and vacuolates, and we have frequently had occasion to notice, both in the healthy processes and in the morbid, that the vacuolation may be accompanied with the production of a waste cell. But, where we have the formative excitation outrunning the functional, and the cells produced relatively so fast that they accumulate in papillary processes or in more layers than one, the secretory change is not so obvious. It is shown only in the altered shape and proportions of the cell. In all such cases of hyperplasia belonging to the stage or degree of mucus production the secreting cell tends to become an oblong, staff-shaped, or spindle-shaped cell, composed almost entirely of nucleus, and with little or no cell-substance. Among those pathological processes in the mamma, a whole lobulus is sometimes found in which the acini are lined with long, narrow, staff-shaped nuclear bodies.* In the figure now being described it will be seen that they are mostly spindle-shaped. In the lowest layer a large pyramidal cell occurs, with three nuclei.

The spindle-cells as waste cells of the secretion.

This kind of transformation of the epithelium is the case where the whole cell becomes a waste cell, and has the property of metaplasia or heterology inherent in it. The arguments used at a former stage of the inquiry need not be repeated here. But the present case affords more objective demonstration that those cells belong to the class of waste products of the secretion. An exaggerated degree of the appearance in Fig. 16, on page 148, which is taken to show the passage through the tissues of waste cells in healthy evolution, is constantly met with in these preparations; and the significance of this kind of cell occurring outside the acini is made all the less ambiguous by the fact that the unmistakeable waste cells are found side by side with it. Thus, a large collection of the yellow cells may be seen penetrating in all directions among a group of acini, and forming broad circular belts between them. Collections of the small round cells are also found completely obscuring the outlines of the acini among which they lie. And if the spindle or staff-shaped cells are found in the same positions, that circumstance, taken along with the fact of their excesssive production in the acini, puts it almost on the footing of actual demonstration that they belong to the category of waste cells of the secretion. Now, in those parts of the diseased mamma which constitute the more circumscribed tumour nodules, a great part of the bulk of the tumour consists of such aggregates of elongated nuclear cells between the acini, and the larger those inter-acinous collections of cells are, the more do the outlines of the acini become obscured, till in well developed parts of the new growth they lose their individuality altogether. If the disease or the tumour is in an earlier stage than this, it will probably correspond to an "adeno-sarcoma" the "sarcomatous" element being represented by the spindle cells outside the acini, and the "adenomatous" element by the cells than are still *in situ*.

Criticism of the term "cystic sarcoma."

The term "cystic sarcoma" probably corresponds to the same pathological condition of the mamma. It has long been an objection to that term that there is nothing particularly cystic in the ordinary sense of the word, in most of the tumours to which it is applied; and if the preceding statements are not overthrown, it will be an additional objection to the name that the tumours are not at all "sarcomatous", a connective-tissue origin being necessarily implied in that term.

A mammary tumour made up chiefly of spindle cells.

Many parts of the smaller nodules, as has been said, show that particular degree of the pathological process in which the elongated or spindle-shaped nuclear cells are crowded about the acini, which are still entire. But the whole of the large tumour, which was a soft whitish

* An appearance of this kind is figured by Langhans, *Virchow's Archiv*, Vol. 58, Plate 3, Fig. 4.

globular mass about 3 inches diameter, represents that state of the mammary tissue, where it is so crowded with the spindle cells that the acini cannot longer be distinguished individually. Fig 33 is a drawing

Fig. 33.

From a mammary tumour in the bitch. Broad tracts of spindle cells enclosing alveolar spaces containing other forms of cells and mucus. Magnified 300 diameters.

from a portion of the tumour. The tracts of spindle cells may be seen to follow a sort of figure-of-eight direction; there occur at pretty regular intervals among them lighter alveolar spaces in which the cells are of more cubical shape and thinly scattered, and in those alveolar spaces there is usually seen a homogeneous or granular ground substance which in some cases resembles mucus. The tumour would probably be classed as a myxo-sarcoma. There is everywhere evidence of a rapid multiplication of the tumour cells *in loco*, but there is no reason to suppose that the origin of the growth was a proliferation of the connective tissue cells of the part. There is no doubt a settled conviction that spindle cells are always the derivatives of the connective tissue corpuscles, and the above account of the tumour in question will probably appear at first sight to have entirely overstepped the bounds of pathological orthodoxy, and to belong to that class of audacious judgments which the French call *saugrenu*. But in the last resort there must be an appeal to the facts and to the correctness or the reverse with which they are interpreted. No other consideration need have any weight except the consideration that "good reasons must, of force, give place to better."

Further illustrations of pathological processes in the breast: myxomatous and cartilaginous tumours.

We now come to the last group of illustrations of pathological processes within the mamma. They relate to those "myxomatous" tumours that have a tendency to become cartilaginous, and the illustrations are all derived from the cases in the bitch. The frequent occurrence of cartilaginous tumours in the mamma of the bitch is well known. In the present series of cases, which includes all the tumours in the bitch that were

treated at the Brown Institution during two years and a half, the proportion of cases that show more or less of the cartilaginous structure is more than one-third, and a still larger proportion of cases exemplify those earlier pathological processes of which the cartilaginous transformation is the final and comparatively safe issue. Thus, a case occurred in which the new growth reappeared at several points in the chain of glands about a year and a half after the removal of the original tumour. The nature of the latter can only be guessed at; it is described as being a globular mass of firm consistence. When the animal returned, the greater part of the mamma was affected, more or less uniformly; there were also enlarged glands in the axilla, and the lungs were discovered to be full of soft white tumours. The structure of the secondary tumours was quite definite, and could be at once referred to that kind of primary tumour of the mamma represented in Fig. 27, on page 185. The secondary structure consisted of round or elongated acinous spaces, the walls of which were covered either with several layers of epithelium of the nuclear kind, or with knob-like processes of the same kind of cells. Now, those parts of the mammary recurrent tumour that were examined did not show precisely the same appearance. One point was distinctly cartilaginous, and going on to a further osteoid transformation, while the other parts chiefly belonged to the kind of growths about to be described. The infection of the lung had been derived either from a part of the gland where the pathological process remained simple and uncomplicated, or from an earlier stage in the progress of the mammary growth generally. It may be safely said that a pathological condition of the mamma which had advanced towards a cartilaginous formation, would not be likely to infect any of the distant organs that are liable to be the seats of secondary tumours.* The notion that one gets from this case in a circuitous way that the cartilaginous structure is the comparatively safe issue of earlier pathological processes in the mamma, is well borne out by direct observation of other cases. The change or modification of the excitation itself, which carries the process to its comparatively safe issue, can only be guessed at. It has been already mentioned that in the case of recurrent malignant tumour figured on page 195, the tumour removed two years before was of the kind that tended to the cartilaginous issue. The disease when it first appeared at one small part of the mamma ran a course to a comparatively safe termination; but in the interval almost the whole of the gland became affected at many different centres, and the issue of the process, although at one or two points it was the same as before, was for the most part a malignant form of tumour. Whatever other controlling causes may have been at work to bring about so important a difference, the lapse of two years, being the increase in the age of the animal, must be kept in view. One might say that the entire forces of the organism would become greatly modified during two years of the life of an old animal; and as we have been led by the evidence to view the excitation to the mammary disease as a spurious awakening of one of those forces, and to regard this abnormal evolutional force as acting upon the gland with a feeble intensity for an indefinite time, so we are led to expect that the lapse of time will modify the effects of the spurious force itself. The actual result is that the waste products of the secretory excitation are more purely cellular and heteroplastic.

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* The tumours of the parotid, partly myxomatous and partly cartilaginous, have a general resemblance to the class of mammary tumours above referred to. The parotid tumours are known to be comparatively innocent growths, which may have existed for many years without infecting the system.

The particular cellular changes, by which the pathological process is conducted to its cartilaginous issue, are fortunately capable of being traced out in a satisfactory manner. Fig. 34 is a drawing of several

Fig. 34.

From a mammary tumour in the bitch. A group of four acini, showing various changes of the epithelium. Magnified 240 diameters.

contiguous acini from a case that had the cartilaginous tendency in a very marked degree. The large principal tumour was partly cartilaginous as well as partly osseous, and the smaller nodules exemplified other processes as well. The fringes of the more or less normal mamma showed exquisitely the process of pigment-cell formation in the acini, and many parts of the tumours had immense numbers of the large yellow cells in the fibrillar tissue. But the pathological processes, as a whole, have their type in the later stages of the normal evolution. One of the acini in the figure will be found to have a trabecular growth within it not unlike those already described ; another shows a papillary process, while the whole of them show an unusual condition of their epithelial lining. The marginal row of cells are round nuclei of considerable size embedded in some intercellular substance. In that respect the condition is the same as in the other cases of many-layered hyperplastic acini. But the condition in the lower layers is completely different, and it is in the differences exemplified there that the special characters of the process now under consideration consist. That difference may be said in a word to be the more real vacuolation of the cells, corresponding to a greater intensity of the functional stimulus.

In treating of the pathological processes to which the last described tumour is to be referred, it was mentioned that the perfect mucus cells were elongated cylinders, that an entire lobulus was sometimes found in

Rod-shaped or filiform cells resulting from a functional change in the epithelium.

which the epithelium was in the form of long narrow rod-shaped cells, and that the elongated or spindle form of the epithelium was especially well-marked where there were more layers than one. The perfect mucus cells as drawn in the pair of acini already mentioned had a nucleus at their attached end and a large amount of granular cell substance, but the filiform or rod shaped, or spindle shaped cells of the pathological acinus were chiefly nucleus, and had little or no cell substance. The last fact was taken to indicate that the cells had undergone a certain degree of functional transformation; that they were not perfect epithelial cells, but in reality the waste products of the secretion. Whatever secretion proper they had given origin to was in the form of intercellular substance, but otherwise it might be said that the whole epithelial cell became waste. Now, the position that has to be advanced at this point of the investigation is, that a very common class of slender rod-shaped or crescentic bodies found in the particular pathological processes at present under review, are phenomena of the same class. The acini in Fig. 34 show several of these. In many cases the dark coloured crescentic line evidently corresponds to only one side of a cell or of a nucleus; it represents in fact the peripheral solid part of a cell undergoing that degree of vacuolation which is represented in the figure on page 131. The peculiarity of the pathological process is that the vacuolation does not result in the production of an actual fluid which is discharged, but of a *hyaline intercellular substance*, among which the dark coloured straight or curved bodies, as well as paler round nuclei

The hyaline substance of enchondromata is an epithelial product.

Fig. 35.

From the same case of mammary tumour as Fig. 34. A group of acini distinguished by their hyaline appearance. Extensive vacuolation of the epithelial cells: hyaline contents of the vacuoles. Magnified 240 diameters.

lie. This account of the process will become much more intelligible and will doubtless gain in credibility by a reference to the next figure, which is taken from the same case as the preceding. The acini contain

a number of large cells resembling fat cells. But the appearance in the preparation, although the woodcut may fail to give it so completely, is not that of cells filled with fluid, but of cells filled with a solid hyaline substance. The cells are in fact the vacuolated epithelium; the hyaline substance corresponds to the contents of vacuoles, and the crescentric or rib-shaped bodies to the peripheral masses. The figure might be matched with another almost similar from a different case, and in the latter there may be seen in the immediate neighbourhood of the hyaline-looking acini, an acinus in which the cells round the wall have the ordinary appearance of vacuolated cells with a peripheral mass of considerable size. It is quite exceptional, however, to find the thin crescent-shaped or fibre-like bodies in their original relation to a vacuolated cell, and there is reason to think that the functional change to which they are due is often not an obvious vacuolation at all. They are generally found scattered among nuclear cells and in a hyaline matrix. Isolated in this manner, they are apt to be mistaken for the fibres of the connective tissue framework in which epithelial cells are supposed to be set. But besides their relation to vacuolated cells, there is another position in which they are found that may clear up any doubts as to their real nature. One of the acini in Fig. 34 shows a trabecular band stretching across it, and the appearance is not uncommon in this and other cases. Sometimes the trabecules are much narrower than that in the figure; the free space of the acinus is bridged over by a sort of network. Those trabeculæ at once suggest the trabeculæ already described in two cases of cancer of the human subject. In the present case they are made up of long rod-shaped cells and a quantity of hyaline intercellular substance; the principal difference between them and the trabeculæ of the other case, is that their cells are longer, narrower, and almost like fibres; but that is a difference that is quite in keeping with the altered circumstances of the case.

Papillary growths in the acini and ducts.

The last two illustrations have been, for obvious reasons, selected to show the pathological process within acini that are simply enlarged; the new growth so far depends on collections of cells in the lumen of acini, on several layers of cells round the wall, or on trabecular bands filling up the space more or less. But although the peculiar transformation of the individual cells is everywhere the same, that change in the cell is not, as a rule, associated with simple enlargement of the acini. Perhaps the most characteristic feature of these tumours is the growth in the acini (and in the ducts as well) of papillary and bud-like processes, which sometimes reach an enormous size. The bud-like growths are attached to the wall of the acinus by a short pedicle; the expansion of the process is globular, and sometimes its free extremity bends over, and, as it were, grows downwards again. The dilatation of a single acinus by such an excrescence is sometimes very great. The free border of the growth is lined by a row of the round nuclear cells separated by some intercellular substance; the appearance is the same as in the marginal row of cells where there are several layers in the acinus, and the appearance in the centre of the bud-like prominence corresponds also to that of the lower stratum of cells. Where the process is well advanced, the substance of the intra-acinus or intra-canalicular papillary growth is made up of a hyaline matrix with a number of round nuclei, and many of the fibre-like or crescentic bodies embedded in it. But papillary processes may be seen which are almost entirely cellular, with some intercellular substance, and others, again, seem to be made up almost entirely of a mucus-like homogeneous substance which stains deeply. Another kind of papillary process has an arborescent structure running rather to the length than the breadth, and these are the cases

where the filiform or rod-like cells are most abundant. How these various structures become true cartilage is not easy to make out, although the fact is undoubted. If a portion of the tumour that has the naked-eye character of cartilage be examined, it will often be found that the cellular elements are quite indistinct in the midst of the hyaline matrix, and the common appearance is that of the crescent or rib-shaped dark-coloured bodies forming one side of what obviously corresponds to the future cartilage cell. The most probable explanation is that the pale nuclear cells, of which a number are to be seen in the acini in Fig. 35, represent the nucleus of the cartilage cell, and that the dark-coloured rib-like lines correspond to the capsule; but that is by no means certain. The origin of the hyaline intercellular substance or matrix has been already explained. Finally, there is not an unfrequent development of the cartilaginous tissue into osteoid tissue. The preparations show perfect examples of medullary spaces (*Markräume*) lined with osteoblasts, and bone trabeculæ containing the same in their substance.

Osteoid tissue.

The pathological processes that we have been last discussing correspond, at least in their earlier stages, to those tumours of the breast that are described as "intra-canalicular papillary fibroma," and "intra-canalicular polypous myxoma." In addition to the statement that the polyp-like growths develop more commonly in the acini than in the ducts, the present account of their histogenesis is radically different from that usually given. But if anyone takes the trouble to look into the current explanation of these growths, he will find that it is based less upon a detailed following out of their development than upon a general pathological application of the law which derives all structures of the connective tissue series from one or other of the various equivalent tissues of that series. So little care has been taken to prove that those new growths of the mamma do actually fall under that law, that the acceptance of the doctrine would appear to be based upon the mode of proof which has been introduced into logic under the name of "the inconceivability of the opposite." The law of the continuity or equivalence of the tissues is no doubt one great law of cellular growth, but, in addition to the principle of continuity, Virchow has himself formulated and given examples of the important principle of "metaplasia." Throughout this research we have constantly had occasion to argue that the cellular products of vacuolation or endogenous cell formation, or of the more obscure forms of activity in the secreting cell that come under the same law, are all of them "metaplastic;" and there is no further effort of belief needed to accept the fact that the secreting epithelium, and not the connective tissue, is the source even of so alien tissues as the myxomatous and the cartilaginous and the osteoid.*

Defects of the systematic method of treatment.

In making use of the 27 cases of mammary tumours which had been collected as the material of a systematic investigation, two courses were open to follow. Either the tumours might have been fully described one by one, with all their attendant circumstances, or they might have been

* In a previous communication (*Anatomical Research towards the Ætiology of Cancer*, Report of the Medical Officer of the Privy Council, 1874) the writer has argued that the cells of secondary tumours in the liver, whether the primary tumours were sarcomatous or lymphomatous or other, were in all cases alike derived from the liver cells by a process of vacuolation or endogenous cell formation. In the formation of the metastatic tumours, the endogenous mode of cell formation was attributed to some unknown "spermatic" or infective influence emanating from the parent tumour. The primary tumours of the mamma are held to be produced according to the same metaplastic law of cell formation, but in the seats of primary disease that law is the inherent law of the function and the diseased process is only a modification of it.

used collectively to illustrate the various points of tumour formation. The latter course has been the one followed, and it can be confidently stated that the illustrations of pathological processes that have been given in systematic order do not omit the leading facts of any one of the 27 cases. But the systematic method has its obvious defects; the real tumours differ from the pattern or from their physiological type in many small particulars. Perhaps the most common source of their motley appearance is the fact that different processes, each of which is intelligible in itself, may be going on side by side; and that circumstance, which is invaluable for explaining the histogenesis of a new growth, makes it less easy to give a succinct account of its morphology. If the tumours were all to receive names, the names would require to be of a highly composite kind. "Adeno-myxo-sarcoma" or "Adeno-myxo-enchondroma," with additional adjectives for pigmented parts or for osteoid parts, would be, after all, incomplete descriptions of a prevalent kind of tumour in the bitch. As to the tumours of the human subject, a rapid survey of them one by one will supply some of the omissions in the preceding account.

Survey of eight cases in the human subject.

The tumour of the male breast need not be referred to again. The "medullary" tumour of the female breast, of which drawings have been given, may be dismissed briefly. The patient was 62 years old; the disease was limited to an outlying part of the gland; the rest of the mamma was very firm, and composed almost entirely of dense felt-like tissue, among which the remains of gland structure occurred at wide intervals. That would appear to be a usual condition of the breast in women beyond the climacteric period, and it enables us to understand the peculiar hardness of the tumours that usually occur in the breast at that time of life.* A skirrhus would consist largely of an infiltration of the felt-like tissue with a certain number of cells derived from the remnants of the gland structure proper. The tumour in this case, however, belonged to the medullary class; it was not an infiltration, but a circumscribed and somewhat soft nodule. It was composed entirely of enlarged acini within which was a development of cells that has been minutely described already. It remains to add that there was a good deal of free pigment of a yellowish-brown colour in the fibrillar tissue outside, and that the free space of the acini, where such existed, was often occupied by red blood corpuscles, and by a number of large vacuolated cells. The latter appeared to be derived from the uppermost of the many layers of epithelium lining the walls of the acinus, and to be the nearest approach to the perfect functional activity that any of the epithelial cells reached. The large vacuolated cells are the well known mother-cells of cancer. Sometimes they contain several small young cells in their vacuole, but others of them have merely the peripheral mass of the vacuolation process, and some of them are little more than the indistinct rings of cells that have been vacuolated more extensively.† Before

The "mother-cells" of cancer

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* "Thus we are told that scirrhus is marked and distinguished by its fibrous character; "whereas the fibrous appearance, in a great degree, belongs to the normal condition "of the organ, and is not a product of the disease. Many other equally erroneous "statements might be mentioned, and for this reason I felt that it was absolutely "necessary to give an account of the natural structure of the breast, before its morbid "changes could be properly explained or understood."—Astley Cooper, Introduction to *Anatomy of the Breast.*

† This more or less complete vacuolation of the epithelial cells is doubtless the fatty metamorphosis or degeneration of cancer cells, which Virchow has shown (*Archiv*, Vol. I. p. 138) to lead to a partial healing of the disease. It is only another mode of expressing the same fact to say that the (more or less complete) vacuolation

leaving this case of medullary cancer, it is to be noted that it occurred at an age when the soft and circumscribed tumours of the breast are not usually met with. The peristenee of some outlying part of the gland in a less atrophied condition than the rest must perhaps be assumed to account for the fact.

Three more of the cases in the human subject belonged to the softer varieties of cancer. One of these occurred in a widow aged 36. The disease was at first circumscribed and situated in an outlying part of the gland, but it spread rapidly and the tumour ultimately protruded through the skin as a fungus. The cells throughout were of the same large nuclear kind as in the last case, with the addition that multinuclear or giant cells were not uncommon. There was the usual intra-acinus growth of cells, but there were besides, extensive columns of cells in the tissue outside. A large part of the adjacent mamma was obtained for examination. One cluster of greatly enlarged acini was found which showed a distinct approach to the structure of the tumour, but the mamma generally was little removed from the resting state. There was no production of pigment cells, as in the bitch. In the second of the three cases, the clinical history was not ascertained. The growth consisted of large and very regular lobules, separated by narrow tracts of fibrillar tissue; each lobule was made up of a large number of acini of a uniform size; the acini were small and were completely filled with a number of the same large nuclear cells as in the other cases. The third of the cases occurred in a married woman aged 39. Parts of the gland within the tumour area were found little affected; those parts consisted of lobuli in an extreme state of involution, separated from each other by wide tracts of fibrillar tissue. The lobuli were made up of a number of lateral offshoots or infundibula from a central duct; the cells were of the nuclear kind always found in the resting state of the gland. The growth itself was almost entirely intra-acinus. The acini were not very greatly enlarged, and the cells within them were more of the kind that are found in myxomatous tumours than in medullary cancers; that is to say, they were often staff-shaped or crescentric elements lying among a homogeneous or fluid substance.

Carcinoma alveolare.

The last mentioned case affords a convenient transition to the four remaining tumours of the human subject which may be called skirrhous although they were not all of equal hardness. One of them, from a widow aged 40, was a good example of the kind of hard cancer in which the cells are contained within alveoli and appear to be suspended in a clear fluid. In this case also the forms of the cellular elements resembled those found in the processes of myxomatous transformation, and which have their physiological type in the mucus-producing stage of evolution. Frequently a large nucleus lay as it were free within a cell which had one part of its wall thicker than the rest. The

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of some of its epithelium is the nearest approach to the healthy function that the gland attains to under its diseased circumstances. The peculiar "bird's-nest" appearances of epithelioma of the skin are phenomena of the same kind. The hyperplastic processes of the cells of the *rete mucosum* may be supposed to have an imaginary lumen, so that the central cells of the process encircle this lumen, and are the most superficial of the several layers round about it. The superficial cells of the normal *rete* tend to undergo characteristic functional transformations, either the horny transformation of the epidermis or the fatty transformation of the sebaceous glands; and these are precisely the transformations that produce the appearance of the "globe épidermique." This appearance shows that the functional tendency is not wanting in the cells composing the hyperplastic offshoots of the *rete*.

crescent-shaped peripheral masses were also found separately.* The fluid in some parts took on the logwood staining almost as deeply as mucus. The cancer juice, as is well known, is more a serous than a mucous fluid. In several cases in the bitch, which did not differ in the firmness of their texture and in other respects from the cancers of the human subject, the fluid that escaped from the cut surface was of a brownish colour. The difference between that kind of "cancer juice" and the kind usually found in skirrhus of the human subject is perhaps the difference that has lately been established between the "mucous" and "serous" condition of the secreting cells of parts of the digestive tract. This particular case of alveolar cancer also showed very well the "small-celled infiltration" of the stroma, which had the appearance of a tissue the subject of chronic inflammation. A sort of chronic inflammation is usually said to be the cause of the phenomenon, the cellular elements being the escaped white blood cells, but it is certain that in many cases of tumour of the bitch, the interlobular and inter-acinous fibrillar tissue is occupied by large numbers of round nuclear cells which are evidently the waste products of the secretion or their derivatives.

The cancer juice.

Small-celled infiltration of the stroma.

The second of the group of hard cancers differed slightly from the last mentioned. The patient's age was 56. The acini showed sometimes the trabecular arrangement of the cells within them, and the interlobular tissue of the gland was in the form of fat tissue which extended in pointed processes into the tumour area. In the third of the group the patient's age was 54. It showed an excessive amount of the small-celled infiltration. The epithelial structure was represented by small areas, each containing a cluster of large vacuolated cells. The corresponding area was sometimes occupied by a concentrically laminated "sand-body," which stained bright purple with the logwood reagent. These bodies have also been observed in one of the tumours in the bitch, and a ewe's udder employed in the study of the normal evolution contained a great many of them, each body lying within an acinus, and almost filling it.†

"Sand-bodies" in cancer of the breast.

The last case of hard cancer is that referred to and figured on page 181. The figure represents waste cells in the fibrillar tissue, but a considerable part of the mass corresponds to gland structure proper, which is itself occupied by the waste products of the secretion.

We have already seen from the cases in the bitch that the earliest and most general disturbance in the mamma is a kind of spurious evolution from the resting state. Speaking generally, the whole chain of glands is equally subject to the first degree of excitation; what distinguishes the portion or portions in which a tumour forms is that the spurious excitation passes on to other stages of the evolution process, notably to the stage of mucus production, and that the cellular waste of the process tends to remain at or near the place of its formation. The distinguishing feature of the less malignant form of tumours is that the spurious secretory activity comes nearer in the degree of its intensity to that of the

The less malignant forms of tumour.

* The account given by Johannes Müller (*Ueber den feineren Bau der krankhaften Geschwülste*, p. 5) agrees exactly with the appearances observed in this case. "In "*Carcinoma alveolare* the walls of those old cells that contain the generations of "young cells appear at last to break up into quite isolated fibres, which have little "connexion with each other."

† The occurrence of "Sandkörper" in cancer of the breast is recorded by Ackermann (*Virchow's Archiv*, vol. 45). The case in which they occurred is described as a case of *Carcinoma atrophicum;* and so also might the above case, from the extreme vacuolation of its cells, and the enormous preponderance of the small-celled infiltration.

perfect secretory activity of the organ ; the vacuolation of the epithelium is a more real vacuolation, and the cellular waste is reduced, in part at least, to the class of fibre-like or crescentic bodies that characterise the myxomatous and cartilaginous issues of the tumour process. The atrophic or regressive cancers of the human female breast may be said also to depend on a more real vacuolation of the glandular cells.

The less affected parts of the mamma in a case of tumour.

But those parts of the chain of glands that do not become the seat of tumours are not always found in the condition that we identify with that of early evolution. In one case, in particular, where the tumour was a large soft mass with the same structure as the medullary cancer of the human subject, the surrounding fringes of normal mamma had the parenchymatous consistence of the well-developed gland, and, on examination, were found to have either the perfect acini with mosaic of polyhedric epithelium, or acini of somewhat smaller size with a more nuclear variety of cells. This case is the only one, in the series of cases from the bitch, in which the mamma may possibly have become affected with the diseased process when it was in some other condition than the resting state. It may very well be that the disturbing force, whatever it was, befel the gland when it was at an advanced stage of the ordinary evolution ; that seems on the whole more probable than the theory that the spurious evolutional force should have simulated the ordinary course of evolution so exactly as to give the whole chain of glands its uniform parenchymatous appearance. In several others of the cases, portions of the mamma surrounding the tumour are found to have the perfect mosaic of epithelium in the acini ; but the lobules of fully-developed acini are mixed with other lobules which illustrate all the periods of evolution from the resting state, as well as the typical resting state itself. Thus, the two varieties of polyhedric epithelium in Fig. 2, are drawn from the fringes of mamma round a tumour, and the lobule in Fig. 4, which is fairly representative of the extreme involuted condition, or the resting state, is drawn from the same case. But the fringes of mamma round the tumour most commonly show the early stage of evolution, and when a more developed state of the gland is found at certain points, the explanation is that the spurious evolutional force has carried some parts of the gland further towards complete evolution than others. In those parts, again, that have become tumours, the cellular activity corresponds also to a stage of evolution that has advanced beyond the initial stage ; but the process has become a pathological process in one or other of the various ways that have been already fully described.

Inflammation and abscess of the breast.

The circumstance that the unknown diseased excitation most commonly befalls the gland when it is in its resting state is of the first importance in accounting for the formation of a tumour. This statement may be made clearer by means of a contrast. When the mamma in its state of perfect development and full functional activity becomes the subject of an interference, the result is very commonly an acute inflammation and the formation of an abscess. Such inflammations are well known to follow on any sudden interference with the function of the breast ; a sudden stoppage of the milk soon after the lactation has been established is apt to produce inflammation, and the same result, or a degree of it, sometimes follows the weaning of the child after a long course of suckling.* The disturbing cause, whatever it may be, acts

* " The mammary glands often become immensely distended at the time of weaning and by manipulation hard knots or lumps are discovered. . . . The axillary glands may become painful, swollen, and even advance to suppuration." Birkett, *Diseases of the Breast*, p. 182.

upon the mamma when its function is at the greatest intensity, and the characteristic effect is inflammation and abscess. The exact nature of the cellular processes that go on in inflammation is still a matter of controversy. According to one view the leucocytes that are found to crowd the inflamed area are derived in every case from the blood vessels, being the escaped white corpuscles; according to another view the leucocytes of an inflamed part may have other origins as well. Now, if reference be made to the figure on page 136, it will be seen that the fibrillar tissue about the acini, and the lymphatic channels encircling them are crowded with leucocytes or lymphoid cells, which are derived beyond doubt from the secreting epithelium. The case was precisely one of those cases where an inflammation of the gland might have been expected; the ewe gave birth to a dead lamb at the full time, and no other lamb was put to it to suck. The figure shows the state of the glandular tissue three weeks after the parturition; there were no signs whatever of inflammation, but it is easy to imagine that a more excessive or more general production of the same lymphoid cells from the epithelium would have led to the appearances of inflammation and of abscess. The small round cells in the figure are the waste products of a somewhat enfeebled secretory activity; they are the characteristic kind of waste product that the epithelium tends to form when the functional excitation is only a little short of its highest intensity. It may therefore be said that a disturbance of the glandular function tends more to transitory inflammations or abscesses and less to permanent cell collections or tumours, in proportion as the secretory excitation is near its highest intensity and the epithelium of the acini near its perfect form. Contrary to the rule that obtains in morals, the pathological case may be said to be one of *corruptio optimi optima.**

Curable tumours of the breast in young subjects

The comparatively safe issue that follows the disturbance of the glandular function at or near its highest intensity affords an analogy for the comparatively safe or curable tumours of the female breast that are apt to occur between puberty and the age of 30 or thereby. They are classed by Billroth under the name of adeno-sarcoma, and their characteristic is said to be that they frequently tend to undergo spontaneous resolution. It is also a familiar fact of surgical practice that the same class of tumours of the breast are sometimes dispersed by strapping or by some irritant inunction or by the application of cold. On the other hand, by far the greater number of the really intractable tumours of the breast are those that occur at or near the climacteric years. The occurrence of that period in the life of a woman affects the mamma both in a positive and in a negative way. The final stoppage of the menstruation is known to produce certain "sympathetic" movements in the breasts; they sometimes even enlarge and discharge a milky secretion. In the class of women who have not borne children and in a large proportion of the child-bearing class the sudden disturbances at the climacteric period are greater than the organ has experienced for years before. But the real fatality of those climacteric disturbances, and

The fatality of the climacteric years.

* A place may be found here for an observation by Sir Astley Cooper (*The Anatomy of the Breast*, p. 137). "Suckling also diminishes the disposition to "malignant diseases of the breast, for although women who have had children are "still liable to cancerous and fungoid diseases, yet it is undoubtedly true, that "breasts which have been unemployed in suckling, in women who have been married "but are childless, and in those who have remained single, are more prone to "malignant diseases than those of women who have nursed large families; "and if it were only to lessen the probability of the occurrence of such horrible "complaints and causes of dissolution, women ought not to refuse to suckle their "offspring."

of all excitations, emotional, mechanical or other, that befall the mamma after that period, lies in the fact that the gland then undergoes a final and permanent involution of its secreting structure. Its framework not only becomes stark and stiff, but there is an absolute loss of that capacity for expansion or evolution which remains throughout the child-bearing period. If, after the climacteric period, the organ becomes the subject of some functional excitation acting upon it through the old physiological channels, the effect is more likely to be the formation of products belonging to the cruder forms of waste cells, which in all probability the lymphatic channels would fail to carry off.

Summary as to the liability of the breast to cancer.

The liability of the breast to malignant tumours may be said therefore to depend on at least three principal circumstances. The first and most important of these is the circumstance that the law of the secretion is the law of endogenous cell formation, which always affords an opportunity for the formation of collateral cellular products, not only useless but also heteroplastic. The second is the circumstance that the gland is liable to periodical remissions of its function, that it remains in an involuted or resting state for a greater or less portion of the mature years of every individual, and that it re-acquires its full development and activity after each period of rest, only by passing through a slow process of evolution. The third circumstance is that a time arrives in the life of every woman, long before old age, when the mamma is no longer capable of reacting as before to the excitations that may befall it, and when the process that may be set up within it is more than ever likely to have a disastrous issue.

In bringing the account of this research to an end, it remains to speak briefly of the method that has been followed and its advantages over other methods. Instead of treating malignant tumours as so many well defined species of new growths that have their seat in various parts of the body, including the breast, the tumours of the breast have been viewed throughout simply as diseases of that organ, and their histogenesis has from point to point been referred to certain particular departures from the normal cellular activity of the gland. The physiological processes of involution and evolution which have been minutely described in the first part of the report, and which are therein explained for the first time, have afforded a greatly enlarged and more adequate basis for the study of the pathological processes. The method that has been followed is not only suitable to the ætiological purpose of the research, but it is a sure means of avoiding a fallacy which is of very common occurrence in investigations and discussions on tumours. Nothing is more common, even in the newer literature, than to find the cancerous tumours of an organ treated as if they were something other than a condition of the organ itself, as if they were separate entities subject to their own laws and endowed with a purpose hostile to the natural life of the part. This fallacy has plainly enough been introduced through the process of abstraction, whereby a diseased condition common to a number of similarly constructed organs has been, in words, isolated from all of them and treated for convenience as an *ens per se*. In the case of the word "cancer" the generalising process has been applied in the usual way, and the abstract name, like other abstract names, is no doubt calculated to be of great use. But it is the fatality of abstract names that they are constantly used in a real or concrete sense, and there could not be a more flagrant instance of their abuse than in the case that we are now considering. Even the definition of cancer has been sometimes made to embody this fallacy. For example, the definition of Johannes Müller runs as follows: "All tumours may be called cancerous which

A common fallacy in treating of tumours.

supersede (*aufheben*) the natural structure of the tissue. . . . . The most general characteristic of cancerous degenerations is loss of the tissue proper of the affected part, which disappears with the development of the cancer . . . . The first appearance of the cancerous degeneration consists, therefore, not in a mere transformation of the pre-existing healthy tissues, but in the development, among the tissues of the organ, of the form-elements of the cancer, which forthwith set aside the natural structure. . . . . The matrix-cells (*Keimzellen*) of carcinoma originate, for example, not from pre-existing fibres, but independently from a true *seminium morbi* which develops among the tissues of the organ."* The following remarkable passage from the well-known work of Paget is an example of the same fallacy in more recent times. "My own experience has (perhaps by chance) been such as would indicate that innocent tumours are less liable to cancer than the structures they resemble; for, as I have elsewhere mentioned, I have seen three cases in which cancer affected the natural structure of the mammary gland, while, close by, mammary glandular tumours remained unaffected."† "Cancer" may affect "the natural structure of the mammary gland," while it spares the adjoining "mammary grandular tumour." The statement can only mean that the pathological process in one part of the mamma deserved, in the estimation of the writer, to be called cancerous, while the pathological process in another part of the gland amounted simply to "glandular tumour" corresponding to the "adenoma" of other writers. But, as the statement is expressed, it succeeds in throwing a veil of mystery over a comparatively simple fact. Having once isolated the disease, in language and in thought, from the diseased organ, we proceed to treat the former as if it possessed attributes or qualities of its own other than the attributes or qualities of the organ. This mistake is all the more readily made because the disease appears itself to have length, breadth, and thickness; which simply means that the disease is characterised by an increase in the length, breadth and thickness of the part. The tumour or swelling of the part comes to be regarded as a sort of parasite on the part; it becomes an *imperium in imperio*, and laws are discovered for it which may perchance be the same as, or may perchance be different from those of the part in which it grows. Looking at cancer of an organ as simply the cancerous condition of that organ, it is apparent that the hardness of a skirrhus of the breast is simply the hardness of the breast or a part of it. If cancer is an attribute or property of a particular organ, it is obvious that this attribute or property cannot have, in reality at least, its own independent attributes, properties, or predicables. Thus, in strict logic, it is inaccurate to speak of the degeneration of a cancer; it is all the while the diseased breast that undergoes the "degenerative" changes. As we have already seen, the degeneration or metamorphosis of a cancer means to some extent the healing of the disease, and we have also seen that the degeneration in the tumour cells is in reality the nearest approach that the diseased gland makes to its healthy action. The degeneration of a cancer of the breast is, so far as it goes, the healing of the diseased breast. If it were once clearly admitted that our common mode of expression is elliptical, there is no reason why it should not be entirely useful and not at all misleading. It is only in the case of tumours which appear to have their independent length, breadth, and thickness, that it has the effect of leading us into a false pathology. The same form of speech is

* *Ueber den feineren Bau der krankhaften Geschwülste*, p. 10.
† *Lectures on Surgical Pathology*, 2nd Edition p. 785.

employed when we speak of the healing of an ulcer of the stomach. Nothing is more convenient than to describe the process of repair in that manner, and it never occurs to anyone that it is something other than the stomach itself that is healed. Now, there are cancerous ulcers of the stomach, which are sometimes found more or less cicatrized. This is a case of healing of the stomach no less than the other. The cancerous ulcer differs from other ulcers—it can be best compared with a follicular ulcer—in the greater collection of cells in the submucosa or among the muscular bundles, and in the different characters of the cells; and it is owing to those differences that it is less seldom healed. But if it did happen to cicatrize, and if the submucous infiltration fortunately became more or less dispersed, the process would not be described as a healing of the stomach, but the case would be called one of atrophic cancer—*Carcinoma atrophicum* or *obsolescens.*

Indebtedness to the writings of Virchow.

The fallacy of the dualism of health and disease has been nowhere more clearly exposed than in the writings of Virchow, first in his *Einheitsbestrebungen in der wissenschaftlichen Medicin*, published in 1849, and afterwards in his *Cellular-Pathologie.* Every system of pathology, he points out, had been based upon the notion that there were in the body the two opposing principles of health and disease: "hie Leben, da Krankheit—hie Welf, da Waibling!" In his Cellular Pathology the cell becomes "the ultimate active element of the living body," no kind of cell occurs in the diseased organism that does not also occur in the healthy, and "another function than the physiological resides not in any "element of the body even under the greatest pathological disturbances. "The most unusual disease brings no new form of function with it." Those are the principles that have been dutifully observed in the method of this research. They are not only the most satisfying and the most inspiring to the intelligence, but they are moreover our only warrant for hoping that we may be able, at some future time, to prevent or control this disease if not to cure it.

No. 5.—Dr. Thudichum's Provisional Statement of further Researches in Physiological Chemistry.

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1.—*Further Researches on the Chemical Constitution of the Brain.*

In the course of the continuation of the researches described in my last report it has been noticed that, in the ultimate watery extract of brain, amongst the bodies belonging to the group of principles which contain four elements—namely C, H, N, and O, there are substances which have the characters of *alkaloids*. They were precipitated by phosphomolybdic acid, tannic acid, iodine, mercuro-potassic iodide, mercuric chloride, and silver nitrate. Their isolation was effected by several of these reagents, more particularly phosphomolybdic acid, mercuric chloride, and auric terchloride. After removal of the precipitants by appropriate means, there remained a mixture of two alkaloids, of which one, crystallisable, little soluble in cold, easily soluble in hot water, was easily recognised as *hypoxanthine*, $C_5 H_4 N_4 O$ and identified by elementary analysis of its silver-nitrate compound, as well as by other characteristic reactions. The *second alkaloid*, easily soluble in water, and somewhat soluble in alcohol, not as yet crystallisable, but remaining as a gum-like mass, was analysed in its combination with auric terchloride, and after a correction for reduced gold, gave the empirical formula $C_{21} H_{28} N_7 O_7$ This formula is a mere preliminary expression of analytical facts aided by conjecture, based upon chemical probabilities. Further researches must decide whether the formula is as stated, or is perhaps more simple and approaches another empirical expression of the same facts, namely, $C_3 H_4 N O$ more or less. The study of this body offers extreme difficulties, in the first place, because it is very oxydisable and gradually reduces the metallic salts with which, on first contact, it forms apparently very definite combinations, and in the second place, because it possesses acid characters, which enable it to retain in combination bases such as baryta. In this respect the alkaloid is in fact characteristic of a new series of bodies, which I shall show to be present in considerable quantity in the human and animal body, namely, the class of *soluble alkaloids having simultaneous acid properties.*

Alkaloids may be defined as bodies derived from typical ammonia, by substitution of compound radicles for one or more of the atoms of hydrogen ; the radicles may be homogeneous or heterogeneous, the typical ammonia may be one, or may be present several times over, constituting a multiple type, which gives rise to the possibility of countless substitutions by compound radicles. The best known representatives of this class are the so-called amines and ammonium bases, obtained synthetically, but the most important are the alkaloids of vegetable origin and great poisoning or healing power, such as the principles extracted from opium, cinchona bark, and nux vomica. Of these bodies above a hundred are at present known to science, and

when we add the bases derived from the animal economy and obtained by other means, we arrive at a number exceeding two hundred. It appears, however, that the definition has hitherto been too narrow, just as the modes of searching for alkaloids were far too one-sided and limited. For alkaloids were supposed to be very insoluble, in water at least, and it is not long since this error was recognised when a few highly soluble alkaloids such as colchicine were discovered. It will now be necessary further to widen the definition of alkaloids, so that the bodies, of which the alkaloid from brain-matter is a representative, may be ranged under it. I have already shown with regard to the phosphorised ingredients of the brain that they possess both basic and acid properties at the same time. The same is the fact with regard to the new alkaloids to be described, they possess most of the combining-powers which are considered to be characteristic of alkaloids, but at the same time they possess combining-powers characteristic of acids. Such alkaloids I have extracted from the muscular tissue in great quantity, from several other tissues of organs, particularly the liver, and from secretions, such as milk and urine. I will again refer to them lower down, after having in this place alluded to a few other matters, some known, some new, extracted from the ultimate watery extracts of brains from animals and man.

Lactic acid is obtained in quantity from the condensed extracts, by ether, after addition of sulphuric acid. With it is mixed *a new acid*, characterised by its giving a precipitate with ferric chloride, in the cold. Another precipitate obtained by boiling seems to belong to a second *new acid*. The first gives a crystalline ammonia salt; the ammonia salt of the second is amorphous. While the lactic acid is being extracted a *crystalline potash salt of an organic* acid is deposited in the liquid, this has much similarity to bitartrate, but differs in particulars. All these bodies occur both in human and animal brains. So does *inosite* of which considerable quantities are obtained by the basic lead acetate process. When these substances, alkaloids, acids, and hydrocarbons, are removed from the brain-extracts, little but inorganic salts remains, and the qualitative analysis of the brain being thus near completion, it is probable that in a not too distant future chemistry will be enabled to approach the problem of quantitative brain analysis with tolerable chances of success.

The extracts, after removal of the substances mentioned in the foregoing, were tested specially for *urea*. None was found. It seems, therefore, that the presence of urea in the brain is indicative of disease. In my report on the chemical relations of Cholera, I have shown that in that disease large quantities of urea occur in the brain and cerebro-spinal fluid.*

2.—*On a new class of Alkaloids as Normal Ingredients of the Muscular Tissue.*

The watery extract of muscular tissue has been the subject of the inquiries of many chemists, amongst them the illustrious Liebig, and many interesting facts were elicited by these inquiries. But a large proportion of the constituents of these extracts entirely escaped the grasp of definite analysis, mainly because they were, for the time at least, uncrystallisable. It was therefore of the greatest importance to me to find that by far the greatest portion of these substances obey the reactions ordinarily considered as *characteristic of alkaloids*. At the same time I

* Ninth Report of the Medical Officer of the Privy Council, 1867.

found that they possess the *collateral character of acids*, just like the alkaloid Nr. 2 from brain described above. When these alkaloids were isolated by the phosphomolybdic process and the precipitates were decomposed in the ordinary manner, by baryta, the product retained baryum in strong combination so that it could not be removed by carbonic acid. These baryum compounds are little soluble in alcohol, and can thereby be fractionally precipitated from their watery solutions. I have prepared considerable quantities of these substances, but their study is complicated and difficult, and definite results cannot be obtained in a short time.

3.—*On a new class of Alkaloids as Normal Ingredients of Milk.*

The whey of milk, after removal of all albuminous matter, also yielded reactions indicative of the presence of alkaloids. One of these was recognised as kreatinine, better known as an ingredient of flesh and urine ; another belonged to the class of alkaloids having at the same time acid properties.

4.—*On new Alkaloids obtained by Chemolysis from Albuminous Substances.*

The foregoing facts induced me to revert to some earlier experiments related in former reports on the products of chemolysis of albuminous substances, and I found that the alkaloids already then recognised as such, could in part at least, be isolated by either the phosphomolybdic or the tannic acid process. When they were separated by the baryta process from phosphomolybdic acid, they were found to retain much baryum in combination. When they were separated by lead oxyde from the tannin, they were found to retain lead, and a great portion remained combined with lead in an insoluble state mixed with the plumbic tannate. The free alkaloids were powerfully alkaline, and gave most of the reactions characteristic of alkaloids in a brilliant manner ; but similar to the alkaloids above described, they reacted with platinic chloride only in very highly concentrated solution, and gave peculiar precipitates with salts of iron and copper. They constituted the great bulk of the syrup which is obtained in the preparation of tyrosine, leucine, &c., and the statement that this syrup contained no nitrogen (Bopp) is shown to be erroneous. One of the alkaloids contained 10·21% of nitrogen, and had the composition expressed by the empirical fomula $C_3 H_6 N O_5$.

5.—*On the Alkaloids in Human Urine.*

Fresh healthy human urine was shaken with a little animal charcoal to collect the mucus and epithelial elements, filtered, strongly acidified with sulphuric acid, and then precipitated by phosphomolybdic acid. The collected precipitate was washed with water containing a little sulpuric acid. It was then decomposed with hot baryta-water in slight excess ; this excess was removed by carbonic acid and boiling, and the filtrate evaporated to a small bulk. On cooling it formed a deposit, which was proved to be *pure urate of baryum*. It was specially proved that it contained no hypoxanthine. The yellow filtrate contained much urochrome, giving on decomposition with hydrochloric acid and boiling uromelanine, uropittine, and evolving smell of omicholic products. It was therefore treated with neutral lead acetate, after this with the basic lead acetate, and ultimately with this and some ammonia. The united precipitates were further treated as will be stated below. The filtrate from the lead precipitates was freed from excess of lead by hydrothion

Method by phospho-molybdic acid.

Baric urate.

Urochrome removed by Pb. process.

and concentrated; it was now free from urochrome, but contained yet two alkaloids, of which one was *kreatinine*, the other an alkaloid hitherto unknown, and to which, on account of its remarkable chemical properties, I give the name of *reducine*.

Kreatinine.

Reducine.

Xanthine

The lead precipitates were united and decomposed by hydrothion. The first watery filtrate was strongly yellow, and on concentration and cooling deposited pulverulent *xanthine*. This was separated from urochrome by filtration, redissolved in boiling water, identified by argentic nitrate test in nitric acid solution, and combined with silver oxyde by treatment of the nitrate salt with excess of caustic ammonia. Filtered, redissolved, and reprecipitated, and burnt, 0·484 grm. dried at 100° gave 0·251 grm. Ag. equal to 51·85 °/₀.

A salt $C_5 H_4 N_4 O_2$, $Ag_2 O$, 2 H_2O, would yield 51·4 °/₀ Ag. The salt without the two molecules of water requires 56·2 °/₀ Ag.

The lead sulphide was further extracted with large quantities of alcohol of 85 °/₀, which on concentration to a small bulk deposited much xanthine, and left urochrome in solution. This urochrome solution was united with the main quantity previously extracted by water. The mixture was proved to be *free from chlorine*, and *free from reducine*. It was now evaporated in vacuo over sulphuric acid, treated with alcohol to separate the xanthine as much as possble, filtered, and the alcohol evaporated. The residue was treated with hydrochloric acid, and yielded *uromelanine* and *uropittine* with all their well-known properties. The presence of omicholine was doubtful.

The mother-liquor from these bodies, suspected to contain some xanthine, was treated with phosphomolybdic acid, and the precipitate obtained was decomposed with baryta. The product dissolved in nitric acid, was precipitated from this by silver nitrate; the compound dissolved in excess of nitric acid on heating, was precipitated from this by excess of ammonia, and *redissolved in a great excess of ammonia*, leaving only some slight impurity undissolved. The solution was boiled to expel the excess of ammonia, and the precipitate which fell during the boiling was isolated, and the silver contained in it determined.

0·039 grm. left 0·0174 grm. Ag. = 44·162°/₀. This compound therefore contained much less silver than the theoretical xanthine compound, or the compound analysed above. On combustion too it behaved differently from the xanthine compound; for it swelled up like a "Pharaoh's serpent," and left a cone of metal, while the xanthine salt burns quietly without swelling up, and leaves a nearly white metallic residue. Owing to want of material the inquiry into this point could not be continued any further.

Reducine.—The filtrate from the lead precipitates described above, as containing this substance and kreatinine was freed from lead by hydrothion, and evaporated to dryness while being stirred on the water bath. The residue was treated with boiling absolute alcohol, and the decoction filtered hot. A voluminous baryum salt remained on the filter, while a yellowish matter dissolved in the alcohol. The former was *reducine-baryum*, the latter mainly *kreatinine*.

Reducine-baryum.—It was easily soluble in water, and after burning left baryum carbonate. On addition to the solution of some nitric acid and silver nitrate a precipitate was produced which immediately became dark and black in the cold. With mercurous nitrate and nitrite it gave an immediate black precipitate; with mercuric chloride it gave a white precipitate which was not changed by boiling; with cupric acetate and boiling, it gave a flaky precipitate which became brown; with Fehling's solution and boiling it gave no reduction.

Analysis of the baryum-compound dried at 100°.

0·4540 grm. gave 0·4520 CO_2=27·092 °/₀ C. and 0·1750 grm. H_2O =4·282 °/₀ H.

0·2628 grm. gave 33·3 c.c. gas normal=15·850 °/₀ N.

0·4490 grm. gave 0·1940 $BaSO_4$=25·400 °/₀ Ba.

	°/₀	÷ At W.	÷ Ba.=1.
C	27·092	2·257	12·2
H	4·282	4·282	23·1
N	15·850	1·132	6·0
Ba	25·400	0·185	1·0
O	27·376	1·711	9·2

If the substance be considered as a monobasic acid, these figures lead to the formula:

$$\left.\begin{matrix} C_6\,H_{11}\,N_3\,O_4 \\ C_6\,H_{11}\,N_3\,O_4 \end{matrix}\right\} H_2O\,Ba.$$

If it be considered as a dibasic acid they lead to $C_{12}\ H_{24}\ N_6\ O_9$ as the formula of the free substance. Of this the molecular weight would be 396, while the molecular weight pointed to by the quantity of baryum is 402.

The foregoing figures and formulæ are given with the reserve imposed by the limited quantity of material; but small changes in proportions can detract nothing from the essence of the new facts. The isolation of reducine has been effected by the application of a reagent of special action on alkaloids. This is the principal proof of the alkaloidal nature of the new body; that it combines with bases after the manner of acids need cause no surprise, as there are many substances known to chemistry which have similar properties; the best known amongst these are the amido-acids, like glykocoll.

Kreatine and Kreatinine.— The alcoholic solution filtered from the *reducine* just described, was evaporated, and the residue extracted with little absolute alcohol to remove kreatinine and leave kreatine; the residue was dissolved in hot water, and decolorised by boiling with animal charcoal. It was then allowed to crystallise, and yielded three successive crops of crystals.

First Crystals—Kreatine.—The air-dry crystals had the appearance of kreatine, and their nature was verified by a determination of the water of crystallisation.

0·4596 gm. dried in vacuo over sulphuric acid, lost 0·5076 gm. or 12·53 °/₀ H_2O. The theory of $C_4\,H_9\,N_3\,O_2$, H_2O requires 12·08 °/₀. The crystals were therefore kreatine. It is known that kreatinine, when freed from its combinations and particularly in warm baryta-water, is easily transformed into kreatine, and these bodies are therefore nearly always obtained side by side in certain proportions.

The second and third crystals were not any further analysed, but assumed to consist mainly of less pure kreatine.

The alcoholic extract supposed to contain the kreatinine was precipitated with alcoholic solution of zinc chloride. The viscous (!) precipitate was freed from mother-liquor, by pressure as far as practicable, redissolved in a minimum of warm water, and reprecipitated by absolute alchohol. Dried over sulphuric acid and ultimately at 100° C., it constituted a highly electric powder. In this the chlorine was determined by two different methods:

(*a.*) By dissolving in dilute nitric acid and precipitating by silver nitrate—

0·5564 gm. dried at 100°, gave 0·3660 gm. AgCl = 16·27 °/₀ Cl.

(*b.*) By fusion with caustic soda and nitre, and precipitating solution with silver nitrate—

0·4720 gm. gave 0·3136 gm. AgCl = 16·43 °/₀ Cl.

The compound was therefore not a kreatinine salt, which requires 19·6 °/₀ Cl. This was further confirmed by the determination of the zinc (in the nitric acid mother liquor from analysis (*a*) after removal of the excess of silver by hydrochloric acid), as carbonate in the usual manner. There were obtained 0·1640 gm. Zn O, equal to 23·15 °/₀ Zn. The kreatinine salt would require only 17·83 °/₀ Zn.

After drying, the body did not completely redissolve in water, but left white flocks insoluble. The filtrate left on evaporation an uncrystallisable salt, mixed with crystals, which were separated by their insolubility in little cold water. The dissolved amorphous body gave with ferric chloride a precipitate, which was permanent on boiling, and thereby reminded of the behaviour of the bodies of the kryptophanic group of extractive acids.

The phosphomolybdic acid process is thus shown to remove from urine several alkaloids, of which one at least is new, *reducine;* another body, *urochrome*, now shown for the first time to be an alkaloid; *xanthine*, known to belong to the class of organic bases; *kreatinine*, also known and mostly obtained as kreatine; and two not yet well characterised bodies, of which the one forms a silver compound, the other a zinc salt, and is precipitated by ferric chloride.

The physiological quantities of these substances are probably not so small as one might be induced to believe from the small quantities actually isolated even from considerable quantities of material by the above process; for the phosphomolybdic precipitate is not very insoluble, and consequently much is lost in the voluminous mother-liquors; these had in the first instance to be operated upon without the employment of heat; but evaporation may in future be tried with certain precautions without fear of destroying the substances above described. The phosphomolybdic acid undergoes some reduction in the urine, which becomes deep green from the admixture of blue oxyde to its naturally yellow colour. It is probable that a portion of the reducine contributes to this effect, and after its oxydation escapes the further steps of the process. Then the baryta process is undoubtebly unwieldy, and likely to produce loss particulary of bodies of the xanthine group. On the whole, however, the process yields a considerable amount of new and useful information which, when, suitably applied hereafter, cannot fail to produce interesting and important practical results.

6.—*Diagnosis of some Reactions of the Bases of the Xanthine Group.*

Xanthine, purchased, dissolved in nitric acid and little water, gave a copious white precipitate with argentic nitrate, soluble in large excess of nitric acid on heating; this remained dissolved for some time after cooling, when a similar solution of *hypoxanthine* was already filled with crystals.

The *xanthine silver nitrate* compound was soluble in large excess of concentrated caustic ammonia, and gave a yellowish clear solution; a little coloured matter remained undissolved. This latter was surmised to be *nitroxanthine silver*, and together with the peculiar smell on first solution in nitric acid seemed to indicate that the commercial xanthine was probably made from guanine.

Xanthine made from guanine by myself behaved in every respect like the foregoing; it was however more yellow, and the part of the silver compound insoluble in concentrated ammonia was more coloured.

The *xanthine obtained from human urine* by the phosphomolybdic process described above behaved just like the foregoing; so also did the body separated from last urochrome by decomposition of this latter with acid, and re-obtained by phosphomolybdic process; the products seemed however to contain different quantities of silver, indicating that the silver compound is not stable.

Guanine extracted by myself from guano, behaved like the xanthines above described, but its silver nitrate salt crytallised a little easier than xanthine from dilute hot nitric acid; with a little more acid however it remained in solution like the xanthine salt.

These bodies therefore resemble each other—

(1.) By their solubility in dilute warm nitric acid.
(2.) Their precipitation from this solution by argentic nitrate.
(3.) The solubility of this silver compound in much warm moderately dilute nitric acid.

But they differ by—

(4.) Hypoxanthine silver-nitrate being quickly deposited in crystals on cooling.
(5) Xanthine-silver nitrate being deposited from a similar solution only after long standing.
(6.) Guanine silver nitrate seems to be deposited at a period later than hypoxanthine and earlier than xanthine.

They further resemble each other—

(7.) By being precipitated as silver-compounds free from nitric acid by a slight excess of ammonia added to the nitric acid solution just described.
(8.) By the complete solubility of these silver-compounds in a large excess of concentrated caustic ammonia.
(9.) By the re-appearance of the silver-compound when the large excess of ammonia is allowed spontaneously to evaporate, or is expelled by heat.

No. 6.—Dr. Baxter's Report on an Experimental Study of certain Disinfectants.

I. Introductory.

App. No. 6.

On Disinfectants, by Dr. Baxter.

Various meanings assigned to the term "disinfectant."

The term "disinfectant" has been, and still is, employed to designate agents possessing one or more of the following properties:

1°. That of checking or preventing certain chemical changes due to the operation of azotised ferments, and seemingly independent of the presence of living organisms. The word "catalysis" is used to specify, without in any way elucidating, the nature of such changes. Examples of them are furnished by the action of emulsin upon amygdalin, of diastase on starch, &c.

2°. That of preventing or stopping decompositions which are causally connected with the presence of organisms. Looked at from the biological rather than the chemical point of view, such changes naturally fall under at least two heads, viz., *fermentations*, occurring in acid media, and attended by the germination and multiplication of torula-forms; and *putrefactions*, occurring in neutral or alkaline media, and associated with the presence and vital activity of schizomycetous organisms.

3°. That of destroying the injurious products of any of the above processes, or of rendering them innocuous to man and the higher animals.

4°. That of destroying the contagia of communicable * diseases, or of depriving such contagia of their specific infective power.

Advantage of a precise definition of the term.

It is desirable, for several reasons, that the denotation of the term "disinfectant" should be more rigidly circumscribed, and thereby rendered more precise. The necessity for some such limitation is recognized by a majority of the highest authorities on the subject. Dr. Parkes, for instance (*Practical Hygiene*, 4th edition, 1873), after enumerating the various senses in which the word is used, goes on to say, "By a third party it is used only to designate the substances which "can prevent infectious diseases from spreading by destroying their "specific poisons. This last sense is, I conceive, the most correct, "and it is that which is solely used here." So, too, in the "Memorandum on Disinfection" issued by the Medical Officer to the Privy Council (1866), "those true disinfectants which permanently destroy infective matters" are distinguished, in a preliminary note, from "those agents which merely arrest the progress, or absorb the offensive products of organic decomposition." By narrowing the scope of the inquiry and placing its objects in a clearer light, a precise definition will pave the way for their more speedy realisation. Again, it fixes attention on the right method to be pursued, the only method by which results of incontestable value as regards practice can ultimately be reached. It enables us to avoid the tacit assumption which underlies the indiscriminate application of the term "disinfectant"

* This word is meant to cover the whole ground which is at present unequally and vaguely distributed between the two epithets "contagious" and "infectious." Every attempt to establish a definite boundary line between their respective provinces rests upon a fundamental misconception of the difference which seems to etinc between the mode of propagation of a disease like syphilis, and of one like typhus. There is every reason to believe, as will be shewn further on, that the difference is one of degree only, not of kind; hence it appears better to use a word, like that in the text, with which no distinctive theory of propagation has been connected.

to substances endowed with the properties mentioned under 1, 2, and 4; for even those authors who eliminate group 3 under the name of "deodorants,"* retain to a greater or less extent the confusion of the remaining three. The tacit assumption is that catalysis, fermentation, putrefaction, and contagion, are fundamentally similar or closely related processes; a view which may be more or less near the truth, but which cannot be regarded as established on a rigidly experimental basis.

The definition of a disinfectant which will be adopted in the following pages is this: any agent capable of so modifying the contagium of a communicable disease, during its transit from a sick to a healthy individual, as to deprive it of its specific power of infecting the latter. This definition at once restricts the problem within clear limits, and does away with much of the vagueness which has hitherto been allowed to cling to it. A disinfectant is only designed to act upon contagious matter after it has been given off by the generating organism, and before it penetrates into a healthy one. The field of usefulness open to it will evidently be wider in the case of diseases communicable at a distance, such as small-pox or scarlet fever, than in the case of those which are usually communicated by immediate contact, such as syphilis.

Methods of determining disinfectant power.

We may reasonably pause to inquire how it is that the meaning of disinfection is so differently understood by different inquirers, and that the term "disinfectant" is so loosely employed by the majority of them. Two causes appear to have contributed very materially to this result: the rudimentary state of our knowledge concerning the intimate nature of contagion, and the difficulty of obtaining any direct test of the real disinfectant power of any given agent. As regards the first point, it is evident that until pathologists have come to an agreement on several fundamental questions, the use of disinfectants must remain to a great extent empirical. So long, for example, as it is doubtful whether the contagium of enteric fever be invariably derived from a previous case, or generated *de novo* in any accumulation of putrefying sewage, the problem of disinfection in that disease must continue vague. So, again, the difficulty of getting at any *direct* test of the efficacy of a disinfectant, in the strict sense of the word, is well illustrated by the following quotation from Dr. Parkes, which marks out the extent of our knowledge, or rather of our ignorance, in this department; he is speaking of the effect produced on the contagia by chemical agents, or heat, or cold, in different diseases: "Our knowledge of this point is "very imperfect, as it is necessarily derived simply from seeing if the "spread of any contagious disease seems arrested by the disinfecting "measures we employ. The experiment is a coarse one, and is con-"ducted under all possible difficulties." It is partly owing to the absence of any direct test that inquirers have been driven to rely upon indirect methods; such methods depending in each particular case on the pathological preconceptions of the individual. He who believes contagion to be propagated by albuminoid principles in a state of molecular change, will naturally lean towards such agents as are capable of precipitating or oxidising albuminous compounds, and will employ these properties as a test of disinfectant efficacy; he who adheres to one form or other of the germ theory, will classify disinfectants according to their action on protoplasm, on fermentations, or on putrefactions.

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* That even this distinction between disinfectants and deodorants is by no means universally observed, may be seen in the following quotation from the article on disinfection in the *Dictionnaire de Médecine Pratique* (1869): "D'une manière "générale on appelle *désinfectant* toute substance propre à détruire l'odeur infecte "qui accompagne la décomposition naturelle des matières organiques, et à assainir "certains lieux ou des matières putrides."

App. No. 6.

On Disinfectants, by Dr. Baxter. Their relation to our views concerning the intimate nature of contagion.

Now although it be true that before disinfection can be made to rest on a thoroughly scientific basis, our knowledge respecting the pathology of contagion must be very much more complete than it is, it may yet be possible to arrive at conclusions of practical value by experimenting with matters which are known to have the power of communicating specific diseases, setting aside for the nonce the question with which of their constituents their infective capacity may be bound up. If a reputed disinfectant be allowed to act on any such material, and the latter be subsequently inoculated, the positive or negative result of inoculation must needs furnish a reliable test of the ability of the disinfectant to fulfil the duty laid upon it. And the practical value of this experimental test will be wholly independent of any theory as to the precise nature of the *materies morbi*. Indirectly, of course, the results obtained may seem to harmonise more nearly with one or other of the views respecting contagion which now divide the field of pathology among them; but such support as they may bring to any of these theories will be accessory and not essential to the primary object held in view. Indeed, the method of inquiry now advocated differs from almost all those which have been hitherto adopted in this very quality of independence of all pathological preconceptions.

It is important to bear continually in mind the characteristic feature by which the contagium or virus of a communicable disease is distinguished from every other kind of hurtful or poisonous matter. The characteristic quality of a virus is not its animal origin, for of its ultimate origin we know nothing; not that it gives rise to a constant and invariable train of symptoms associated with definite structural alterations, for many poisons do the same; but that it is capable of undergoing almost unlimited multiplication when introduced into an appropriate medium, that medium being the body, or part of the body, of a certain animal or animals; consequently, its effects are to a great extent independent of the quantity introduced, dilution lessening the chances of infection, but not modifying its specific characters when it *does* occur. It follows that nothing short of the complete destruction of *all* the virulent matter from which danger is apprehended can guarantee us against the indefinite propagation of the disease which is being combated by disinfection. And further, that the only legitimate test of the effectual disinfection of any virulent substance is its inability, when introduced into a suitable host or medium, to bring about the specific train of phenomena which coincide with its own multiplication.

Difference between contagion and infection only one of degree.

One other point should be premised, which, though not essential to the fertility of the above method in results of practical usefulness, is needed for the due interpretation of those results. This point is the particulate nature of contagia, which has been demonstrated in the case of small-pox, cow-pox, glanders, and ovine variola,* and which may be provisionally extended, as a legitimate hypothesis, to other contagia. The fact that the infective principle of these disorders is neither soluble nor diffusible, carries with it the corollary that neither can it be volatile. This last conclusion is supported by bedside experience; it has been pointed out that were the contagium, *e.g.*, of small-pox volatile, the air surrounding a patient labouring under that disease would constitute an uniformly infected medium into which no unprotected person could penetrate, even for a few moments, without extreme risk. That no such excessive degree of risk is run, confers an *a priori* probability on the view that the contagious principle exists in the air in the same form in which it exists in liquids, viz., in the form of solid particles, and is therefore unequally distributed. But to this *a priori*

* See *Twelfth Report of Medical Officer of the Privy Council.*

probability may be added the evidence of direct experiment. Three diseases which enjoy in the highest degree the fame of being communicable at a distance are small-pox, variola ovina, and cattle-plague. If it be experimentally proved that the contagia of these three diseases are not volatile, the generalisation may fairly be extended, until further notice, to other infectious maladies. This experimental proof has been supplied by M. Chauveau (*Comptes Rendus*, 1871, p. 116). He introduced virulent liquids derived from individuals labouring under each of the three diseases in question into small glass cups, embedded in a sand-bath which was kept at a temperature of 40° C. A small bell-glass was inverted over each cup, and maintained at a low temperature by having its outer surface moistened from time to time with ether. The water in the liquids underwent evaporation, and was condensed on the walls of the bell-glass. Now, supposing the virulent principles to have been volatile, they would naturally have risen with the watery vapour and mingled with the condensed droplets, conferring upon these a specific infective power. But, as it turned out, the condensed water, when collected with a capillary pipette, and suitably inoculated, proved to be entirely free from virulence in every one of the instances referred to.

Importance, as regards disinfection, of media in which contagium is suspended.

Granting that the contagious principle is neither soluble, nor diffusible, nor volatile, and that it invariably consists of particles of extreme minuteness, it follows that all distinction between contagion and infection must cease. The one is communication by direct contact, the other, communication at a distance; but the mode of communication is the same in both cases, viz., the transfer of certain solid particles from the infected to the healthy organism. But this recognition of the unity of the contagious principle must not blind us to the fact, all-important in reference to disinfection, that it may be transferred from the sick to the healthy either by means of a solid, a liquid, or a gas. These three states of matter stand in no closer relation to the contagium than that of media or vehicles; media, in which it may sojourn for an indefinite time without forfeiting its infective property; vehicles, by which it may be carried from the sick to the healthy. This point may be illustrated by the example of small-pox, whose virus may be conveyed in a liquid form, derived from a characteristic vesicle; or as a solid crust from a dried pustule, or a patch of dried mucus on a handkerchief; or, finally, it may be air-borne, or perhaps, more correctly, dust-borne. The virus, in all three forms, retains its characteristic activity; it consists of the same particles; but it is obvious that, as regards disinfection, its susceptibility is not the same. A liquid non-volatile disinfectant might act powerfully on the first, feebly on the second, and not at all on the third. This consideration of the medium in which the virulent particles are suspended seems, as we shall see hereafter, to afford a clue whereby some perplexities may be unravelled and some apparent discrepancies reconciled.

Present inquiry limited to four disinfectants most commonly employed.

The object of inquiry and the method to be pursued having been thus defined, a further limitation is introduced, on the present occasion, by the choice of four only out of the multitude of disinfectants indiscriminately used by practical men. These four are *potassic permanganate*, *sulphur dioxide*, *chlorine*, and *carbolic acid*. The very general preference shewn for these four agents may be ascribed rather to motives of expediency than to any theoretical conviction of their absolute disinfectant power. Reasons of expense bar the employment of such substances as iodine and bromine; the stronger mineral acids are too generally destructive to be entrusted to any but experts, and are, even then, of limited applicability. Again, the four agents in question have been known for years, and rudely tested on a large scale; they have been investigated in various

ways, and dogmatic assertions have been made concerning their relative usefulness; and yet it is singular, when the matter is looked into, how scanty is our knowledge about their real disinfectant power, as tested by the only method capable of yielding absolute results.

In the experiments hereafter to be described, Calvert's purest crystalline carbolic acid was used, dissolved in distilled water. The solutions of potassic permanganate were prepared by weighing the crystalline salt, and dissolving it in distilled water at the moment of use. Chlorine was generated in the usual manner from hydrochloric acid and manganese dioxide; the solution was preserved in a black bottle, duly stoppered, and kept cold. The sulphur dioxide was obtained by the action of concentrated sulphuric acid on copper turnings. The solutions of chlorine and sulphur dioxide were invariably titrated after each experiment; the former with potassic iodide and decinormal solution of sodic hyposulphite, the latter with decinormal solution of iodine. They were always used as fresh as possible, and seldom kept for more than a week.

Contagia chosen for treatment by these agents.

The contagia selected for disinfection were vaccine, the virus of infective inflammation in guinea-pigs, and the virus of glanders. A series of experiments with the virus of ovine variola was projected, but not carried out, owing to a difficulty in obtaining a supply of material for starting the inoculations. It need hardly be said that the choice of these three infective substances was chiefly determined by reasons of expediency. Any results obtained from experiments with vaccine lymph owe their practical value to the pathological affinity between cow-pox and small-pox. Further, vaccine is the only specific virus with which experiments can legitimately be conducted on the human subject. Again, it is one of the few communicable diseases concerning whose intimate pathology we possess definite experimental data of high value. This last advantage is shared by glanders, a disease eminently communicable both by contagion and infection, producing specific dynamical and structural effects, and having the additional recommendation, that while it admits of being studied by inoculation on certain of the lower animals, it is also susceptible of being communicated to man in its most virulent form.

The virus of infective inflammation in guinea-pigs stands in a somewhat different position. For we are able to generate it *de novo;* and so far it cannot be regarded as specific, in the proper sense of the term. But it is endowed with what has previously been noticed as the distinctive mark of a virus, viz., the faculty of undergoing indefinite multiplication in the infected organism. Moreover, it produces pathological results which are tolerably definite and constant, depending only to a limited extent, if at all, on the amount of material introduced. So that, for our purposes, it may be said to resemble the specific contagia more than it differs from them; and it has this practical advantage in its favour, that it can be procured in considerable quantity, allowing experiments to be repeated and varied to a greater extent than those with vaccine or the virus of glanders.

Theoretical purpose of the present investigation.

It may be well to state that the main object of such an inquiry as the present one is to furnish materials for the theoretic basis on which all practical rules for disinfection must rest. We do not certainly know that *any* of the agents habitually employed possess real disinfectant power; we have no experimental data as regards their comparative efficiency and the various circumstances which must modify their operation in particular instances. The present Report can do no more than furnish a nucleus of positive observations, limited in intention and still more in execution, round which facts of the same order may here-

after be accumulated; and fix attention on what is believed to be the right road along which future inquiries of this kind ought to travel.

The ensuing sections will be devoted to the action of the disinfectants already enumerated upon vaccine virus, upon the virus of infective inflammation, upon that of glanders, and finally upon the germinal matter of septic microzymes; the last-named section being an endeavour to ascertain whether an underlying harmony may not be found to exist between the disinfectant operation of the substances specified above, and those other properties which have hitherto been very generally confounded with, or taken as evidence of, their truly disinfectant power.

II. Experiments with the Virus of Vaccine.

Relation of vaccine virus to those of human small-pox and variola ovina.

The principal reasons which led to the choice of vaccine virus, as a test of the efficiency of disinfectant agents, have already been alluded to. The affinity of vaccinia to small-pox gives a high degree of practical value to any experimental results which may be obtained in connexion with it; moreover, it has been more closely studied, as regards its intimate nature, the conditions of its activity, and the specific results to which it gives rise, than any other kind of infective matter.

Difference between their respective transmissibility accounted for: Chauveau's experiments.

The virus of cow-pox is not known to be communicable otherwise than by direct contact or inoculation. There is no instance on record of the disease having been transmitted by aerial infection. In this respect, therefore, it differs *primâ facie* from its congeners, the contagia of small-pox and variola ovina, both of which are believed to be readily communicable through the air. Considering the very close analogies which subsist between these three diseases, there is reason to think that this contrast may be due, not so much to any intrinsic difference between the contagious particles by which they are respectively propagated, as to differences in the amount of virulent matter generated in the infected organism, and in the facilities afforded for the distribution of this matter through the surrounding medium. This view has been very lucidly developed by M. Chauveau. Inasmuch as not one of the three contagia is volatile, infection at a distance can only take place by the transfer of particles derived from the diseased individual to some absorbent surface in the healthy one. Such absorbent surfaces are to be found in the mucous membranes lining the air-passages and the alimentary canal. That the virulent matter is capable of being absorbed from the intestinal surface, and causing all the phenomena of constitutional infection, has been experimentally proved in the case of ovine variola; and this result may reasonably be extended to the two allied disorders. Now when we consider the number of distinct foci, each yielding a large amount of infective matter, distributed over the skin of a sheep suffering from the severer form of ovine variola, or of a man affected with small-pox; when we recollect, further, that similar infective foci exist elsewhere in the body (notably in the lungs of the sheep, where secondary nodules full of virulent particles are often developed) in situations which enable their products to be discharged into the surrounding medium by coughing; we cannot but be struck with the contrast between these two diseases and cow-pox as it occurs after inoculation in the human

subject. The quantity of infective material generated in the latter, though very considerable in relation to the amount introduced, falls very far short of the enormous supply yielded by a single case of ovine or human variola; and what there is, is generated in a situation which absolutely precludes its distribution throughout the environment, at least during the period when the infective power of the contagium is at its highest.

Since the difference between the communicability of vaccinia on the one hand, and small-pox on the other, admits of being thus easily explained, it appears superfluous to go farther afield in search of causes; those enumerated are *veræ causæ*, and they are competent to explain the facts. Accordingly we may assume that the difference is one of degree only, and that deductions from experiments performed with the contagium of cow-pox may be extended to variola.

Nature of media in which the particles of vaccine are contained.

The virus of vaccinia may be preserved either in a liquid or a solid medium. In the former, when lymph exuding from a pricked vesicle is collected in capillary tubes; in the latter, when ivory points are coated with the dry residue of its evaporation. The present series of experiments will accordingly be divided into two groups, one devoted to the action of the disinfectant agents, enumerated above, upon fluid lymph; the other to their action upon dried lymph. The results of the latter group will obviously serve as materials for the estimation of the comparative efficacy of gaseous disinfectants; indeed, it is very probable that "aerial disinfection," when distinguished, as it should be, from the destruction of noxious gases in the atmosphere, is really exerted upon contagious particles embedded in dry mucus or albuminoid matter of one kind or another.

Method of testing the action of disinfectants on liquid vaccine.

The inquiry into the action of disinfectants on the virulent particles suspended in liquid vaccine was conducted in the following manner. Four capillary tubes having been charged from one vaccinifer, the contents of two of these were diluted with an equal volume of half per cent. saline solution (·5 grm. of NaCl in 100 c.c. of distilled water); the lymph contained in the other two was mixed with an equal volume of disinfectant solution of known strength. The diluted and the disinfected liquids were sealed up in separate tubes, and employed for vaccinating a healthy infant; the former being inoculated in three places on the left arm, while the latter was introduced into an equal number of places on the right arm, two lancets being employed for the purpose. The inoculation was performed by scratching, not by puncture. The results were observed and recorded on the eighth day. By adopting this method, several sources of possible error were from the first eliminated. The uniform potency of the lymph within the compass of each single experiment was ensured by its being derived from one vaccinifer. The degree of dilution was the same in the disinfected as in the virgin virus. Finally, the inoculation being performed on opposite arms of the same individual, no difference of idiosyncrasy could vitiate the comparative result.

The difficulty of dealing with such very small quantities of material as are furnished by the vesicles on an infant's arm had to be overcome by a special contrivance. Only four of Husband's tubes, little more than half full, could be obtained for each experiment. It was necessary to devise some means whereby the contents of these tubes could be accurately measured, and mixed with an exactly equal volume whether of saline or of disinfectant solution.

To attain this end the following apparatus was constructed. Two

thermometer tubes of small bore, about 28 centimètres in length, were calibrated with a globule of mercury, and divided into 15 equal parts, each of which measured nearly 1·5 centimètres. Each of these divisions was further subdivided into five equal parts. About four centimètres of the upper end of each tube, and 1·5 centimètres of its lower end, remained without graduation.

The lower extremity of each tube was ground down to a point just large enough to include the orifice of the axial canal. Thus each fractional part of either tube was made precisely equivalent to all the rest. These graduated tubes will hereafter be known as pipettes.

The two pipettes were supported on a stand consisting of a vertical pillar screwed into a heavy plate of metal, upon which a cross bar 30 centimètres long moved up and down, and could be fixed at any height by means of a screw. The two arms of the horizontal bar projected to an equal distance on either side of the pillar. To the extremities of the bar two perforated corks were attached by pieces of very thick, yet flexible, wire: the pipettes were introduced into these perforated corks, by which they were tightly gripped. The capillary end of each pipette was directed downwards, inwards, and forwards. Their distance from the table could be varied by sliding the horizontal bar on the vertical pillar, while the direction of their axes could be altered at will, and retained at any desired angle, owing to the flexibility of the wires connecting the corks with the ends of the horizontal bar. Over the upper end of each pipette, when fixed in position, was slipped a piece of gutta-percha tubing, the other end of which fitted a glass mouthpiece; the two mouthpieces being fixed side by side within easy reach of the operator's lips.

The following are the steps of the process. One pipette is charged with saline solution by suction; the liquid is retained by capillarity. Two of the vaccine tubes are then emptied on to a clean slide, and the minute coagulum, which is often present, is drawn aside with a glass thread. The drop is then cautiously brought under the nozzle of the other pipette and the lymph sucked up. The number of measures which it occupies are read off, and it is forthwith expelled very gently on to another slide. An equal number of divisions of saline solution are added from the companion pipette, and the two droplets are thoroughly mingled by stirring with a thread of glass. The mixture is then introduced into a capillary tube and sealed up. Both pipettes are washed out with saline solution, and the two remaining tubes of lymph are mixed in exactly the same way with an equal volume of the disinfectant solution.

These manœuvres, after a little practice, cease to present any difficulty, though they demand time and trouble. It is very important to expel the lymph from the pipette *immediately* after its volume has been read off; otherwise there is great risk of its coagulating in the tube. Again, the attenuated canal of the pipette, where it terminates in the nozzle, is very liable to become blocked; hence, should the droplet of lymph contain visible particles or coagula, it must be manœuvred in such a way as to keep these out of reach of the suction-current. When the operation is carefully executed, no bubbles appear in either pipette; they should be strenuously avoided, as they impair the accuracy of the measurements.

Experimental inoculations with liquid vaccine.

Three sets of experiments were performed with liquid vaccine, the agents employed being potassic permanganate, chlorine, and carbolic acid. The experiments with sulphur dioxide proved a failure, owing to some chemical change which caused the mixture of lymph and acid to gelatinize firmly in the capillary tubes.

Action of Potassic Permanganate on Liquid Vaccine.

No.	Proportion of Permanganate in the Material inoculated.	Number of Vesicles on Arm inoculated with diluted Vaccine.	Number of Vesicles on Arm inoculated with disinfected Vaccine.	Remarks.
1	·025 per cent.	2	0	
2	·025 „	2	2	Vesicles of the same size on both arms.
3	·05 „	3	3	
4	·1 „	3	3	
5	·5 „	3	0	
6	·5 „	1	0	
7	·5 „	2	0	

These experiments point to a result which stands midway between the exaggerated value ascribed to the permanganate by some authors, and the total repudiation of its claims by others. (O'Nial, for instance, concludes that the permanganate is a useful deodorant, but has scarcely any germicide power.)

It is evident that the proportion of permanganate required to destroy the infective energy of vaccine is relatively large; but that, in such excess, it is capable of doing the work.

Action of Chlorine upon Liquid Vaccine.

No	Proportion of free Cl. introduced into the Material inoculated.	Number of Vesicles on Arm inoculated with diluted Vaccine.	Number of Vesicles on Arm inoculated with disinfected Vaccine.	Remarks.
1	·00185 per cent.	3	3	
2	·00369 „	2	3	
3	·0204 „	2	2	
4	·0408 „	3	2	Lymph is alkaline; contains no free Cl.
5	·07105 „	3	1	
6	·09413 „	3	3	
7	·09413 „	3	1	
8	·1421 „	2	2	
9	·1633 „	3	0	Lymph distinctly acid.

The negative results furnished by the first eight inoculations were unexpected. The lymph, after admixture with the solution of chlorine, was found, in every case, to have retained its alkaline reaction and to contain no trace of free Cl. In the ninth experiment, however, in which the vaccine was satisfactorily deprived of its infective energy, it was found to be distinctly acid after the chlorine water had been added to it. It would appear then that chlorine, unless it be added in sufficient quantity to render the lymph acid, has no appreciable influence in restraining or abolishing its infective power.

Action of Carbolic Acid upon Liquid Vaccine.

No.	Proportion of Carbolic Acid in Material inoculated.	Number of Vesicles on Arm inoculated with diluted Vaccine.	Number of Vesicles on Arm inoculated with disinfected Vaccine.	Remarks.
1	·25 per cent.	3	3	
2	·5 „	3	3	
3	·5 „	3	3	
4	1 „	2	0	Vesicles very small.
5	1 „	3	1	
6	1 „	3	3	
7	1·5 „	2	0	
8	1·5 „	3	0	Vesicles large on arm inoculated with diluted lymph; very small on arm inoc. with carbolized lymph.
9	1·5 „	3	3	
10	1·5 „	3	2	
11	2 „	3	0	
12	2 „	2	0	
13	2 „	3	0	

It is sufficiently evident from these experiments that the presence of 1 per cent. or less of carbolic acid in vaccine exerts no influence upon its activity. When the proportion of acid present is between 1 and 2 per cent., the effects of inoculation are irregular. 2 per cent. seems enough to destroy its infective power with certainty.

Method of testing action of disinfectants on dried vaccine.

The next series of experiments was designed to test the efficacy of gaseous disinfectants upon dried vaccine. The following was the simple method pursued. Six points were charged from one vaccinifer and dried. Some days later, three of the points were exposed to the action of chlorine, sulphur dioxide, or the vapour of carbolic acid. To be able to compare the relative power of these three agents, it is necessary to vary either the degree of concentration of the gaseous medium to which the dried virus is exposed, or the duration of its exposure. The latter variable is obviously more under our control than the former one. In the case of carbolic acid, it is well-nigh impossible to obtain an atmosphere containing a given per-centage of the vapour diffused through it; and the chemical activity of chlorine interferes with its treatment by any such method. Accordingly the time of exposure was alone varied, the virus being always exposed to an atmosphere saturated with the gas or vapour at the ordinary temperature of 60°–65° F.

A wide-mouthed four-ounce glass bottle, with a hollow ground stopper, was used as the chamber in each case. The cavity in the stopper was filled with cork, in which three slits were cut, each sufficiently large to admit and retain the broad end of an ivory vaccine-point. The bottle was filled to one-third of its depth with a saturated solution of chlorine or sulphur dioxide, or with nearly pure carbolic acid. Three points were fixed into the stopper, which was then replaced. The charged ends of the points were thus kept within half an inch of the surface of the liquid, and exposed to the full influence of any gas or vapour rising from it. After exposure for a given time they were removed and preserved apart from their fellows. Two or three days later, the three disinfected points were used to inoculate three places on one arm of an infant, while the corresponding places on the other arm were vaccinated with the virgin points.

Effect of simple desiccation on vaccine lymph.

One trial was made to ascertain whether desiccation over concentrated sulphuric acid would modify the infective power of the dry virus. Three points were kept under a small bell-jar into which a basin of

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concentrated oil of vitriol had been introduced, for 52 hours; the edges of the bell-glass were ground and cemented to a glass plate. On inoculation, the dried points yielded three plump vesicles, exactly similar to those produced on the opposite arm by the three corresponding points which had not undergone any sort of treatment.

Experimental inoculations with dried vaccine.

The three following tables exhibit the results of the experiments made with chlorine, sulphur dioxide, and carbolic acid vapour respectively :—

Action of Chlorine on Dry Vaccine.

No.	Duration of Exposure.	Number of Vesicles on Arm inoculated with Virgin Points.	Number of Vesicles on Arm inoculated with disinfected Points.	Remarks.
1	5 minutes	3	1	The vesicles produced by the virgin points were all large; those furnished by the disinfected points, very small.
2	10 „	3	1	
3	15 „	3	2	
4	30 „	2	0	
5	30 „	3	0	

Action of Sulphur Dioxide on Dry Vaccine.

No.	Duration of Exposure.	Number of Vesicles on Arm inoculated with Virgin Points.	Number of Vesicles on Arm inoculated with disinfected Points.	Remarks.
1	10 minutes	3	0	
2	do.	3	0	
3	do.	2	0	
4	do.	3	0	

Action of Vapour of Carbolic Acid on Dry Vaccine.

No.	Duration of Exposure.	Number of Vesicles on Arm inoculated with Virgin Points.	Number of Vesicles on Arm inoculated with disinfected Points.	Remarks.
1	5 minutes	3	1	No constant difference observed between vesicles furnished by carbolized and those furnished by virgin points.
2	10 „	3	3	
3	15 „	3	1	
4	20 „	3	3	
5	30 „	3	2	
6	30 „	2	0	
7	60 „	3	0	
8	60 „	3	0	

One striking result is manifest from this series of inoculations. It is the very marked superiority of sulphur dioxide to carbolic vapour and chlorine gas, and this under conditions which seem, above all others, to render the virulent particles least susceptible to destructive influences. It is sufficiently obvious that the quantity of chlorine given off into a

room from a basin filled with chloride of lime, or the vapour of carbolic acid generated in a vaporiser, would be utterly inadequate to destroy vaccine virus, and, by inference, the contagium of small-pox, when embedded in a matrix of dried albuminous matter ; and it is not unlikely that the virulent matters for whose destruction aerial disinfection is employed are commonly protected in some such way.

The only experiments relating to the disinfection of vaccine virus of which I have been able to find any record, are those of Dr. Henry (1831), Mecklenburgh, and Dougall. None of these observers appear to have investigated the action of destructive agents upon the dried virus, and some of their results are open to question ; but the exceeding dearth of facts will not allow of any experimental data being neglected.

Results obtained by Mecklenburgh.

Mecklenburgh,* in a preliminary notice, makes the following assertions, without, however, giving any details as to the number of experiments performed or the methods employed : 1°. That the exposure of vaccine lymph, diluted with its own volume of glycerine, to the action of chlorine (under a bell-jar) for several hours, fails to impair its efficacy, as tested by subsequent inoculation. 2°. That pure lymph mixed with an equal volume of the *aqua oxymuriatica*† of the Prussian Pharmacopœia, yields normal vesicles when inoculated. 3°. That lymph similarly treated with impure acetic acid was found to have lost its infective power. 4°. That out of eight children inoculated with lymph which had been mixed with commercial carbolic acid (proportions not given), only three took. The mixture is stated to have reddened blue litmus (?). The promise made by the author to publish an extended series of similar experiments does not, so far as I can ascertain, appear to have been redeemed.

Experiments performed by Dr. Dougall.

Dr. John Dougall, in the course of a very interesting experimental inquiry, published in the *Glasgow Medical Journal* for November 1872 and February 1873, performed 11 inoculations with vaccine which had been exposed to the action of certain volatile media. The method is thus described : " To the separate vapours (contained in bell-jars of a cubic " foot capacity) separate minims of vaccine lymph were exposed for " 24 hours. The dry spot remaining was moistened with glycerine and " water, its reaction taken, and the mixture sealed in capillary tubes " till an opportunity occurred for vaccinating a child with it. All the " mixture was used in one insertion so as to make sure of obtaining its " full effect. The lymph in every instance was at first alkaline, and " the glycerine neutral." Inoculation yielded characteristic vesicles when performed with lymph which had been exposed to the action of the following vapours : carbolic acid, camphor, chloroform, sulphuric ether, and iodine. On the other hand the virus acted upon by chlorine, sulphur dioxide, nitrous acid, glacial acetic acid, and hydrochloric acid, proved absolutely barren. Dr. Dougall draws attention to the important circumstance that the mixture of lymph and glycerine, in every case in which it had retained infective power, was either alkaline or neutral ; while in every case in which it had been successfully disinfected, its reaction was decidedly acid.

The general tenour of these results is in harmony with those arrived at in the course of the present inquiry. The apparent failure of carbolic acid is deserving, however, of a moment's consideration. Owing to an accident the vaccine was exposed to the carbolic vapour for 36 instead of 24 hours. The experiment was performed in hot weather (August). Somewhat surprised at the failure of so powerful an agent, Dr. Dougall

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* *Berlin. Klin. Wochenschrift*, 21 June 1869.

† This is a solution of chlorine, containing about ·4 per cent. of the gas.

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inoculated some lymph to which one per cent. of the acid had been added; the inoculation was successful. In the writer's own words: "If "a minim of vaccine matter is unaffected after being buried for 36 hours "in the heart of a cubic foot of concentrated carbolic vapour, or after "being mixed with the acid *per se* in the proportion of 1 in 50 for "10 days, must not the highly attenuated carbolic vapour, alone attain- "able in practical aerial disinfection, of necessity be powerless to cope "with an atmosphere saturated and smelling with the contagium of "small-pox? Moreover, it is manifest that the comparatively small "quantity of the acid commonly used must in many cases fail to affect "the variolous poison, though incorporated with it by the sanitarian "brush in the usual manner." Of Dr. Dougall's two experiments, that in which diluted vaccine containing one per cent. of the acid produced a vesicle, coincides with the results arrived at during the present inquiry; but the failure of the concentrated carbolic vapour seems unaccountable in view of the results given in the last table. The discrepancy, however, does not suggest any difference of opinion on the part of the present writer as to the practical inutility of carbolic acid for purposes of aerial disinfection.

Henry's experiments on vaccine lymph.

Dr. Henry's experiments (*Philosophical Magazine*, vol. X., 1831) were solely intended to ascertain the disinfectant influence of heat on vaccine. As a brief series of similar experiments was performed in the course of the present investigation, it may not be amiss to recapitulate his results; for though few in number, and buried in an almost inaccessible volume, they have long served as the sole experimental basis of disinfection by means of dry heat.

1. Vaccine lymph on bits of glass was exposed to a temperature of 180° F. (82° C.) for four hours. Of three children vaccinated with this lymph none took the disease. They were all subsequently vaccinated with success.

2. Lymph heated for four hours to 120°–140° F. (49°–60° C.) was inoculated in two cases; neither took the disease.

3. Recent lymph heated from two to three hours to 160°–165° F. (71°–74° C.), proved ineffectual when inoculated.

4. Lymph heated for 2 hours at 150° F. (66° C.)
„ 4 „ „
„ 2 at 172° F. (78° C.)
„ 4 „ „
} was found to have lost its infective power.

5. Lymph kept at a temperature of 120° F. (49° C.) for three hours was inoculated in two cases. Characteristic vesicles were produced in both.

Action of heat upon dried vaccine.

Ten inoculations were performed in the course of the present inquiry with dried lymph which had been exposed to heat. The following was the method pursued. A long mercurial thermometer with a cylindrical bulb was fitted into a large test-tube by means of a perforated cork, the bulb of the instrument being fixed in the axis of the tube and close to its lower end, but without touching its walls at any point. The test-tube was plunged into a water bath, and held in a vertical position by a clip. It was found possible, with a little care, to keep the temperature of the instrument nearly constant by varying the depth to which the tube was immersed in the bath. The apparatus was watched during the entire period of each experiment. Three points, folded in tissue paper, were tied on to the bulb of the thermometer in such a way that the charged extremity of each point was only separated from the surface of the bulb by one layer of the tissue paper. The time at which the tube was introduced into the bath was noted, also the moment at which the mercurial column reached the minimum and the maximum temperatures within which the exposure was meant to be restricted; also the

moment of removal. The heated points were used to inoculate three places on one arm; three other points, charged with lymph from the same source, were used to inoculate the corresponding places on the opposite arm.

Action of Heat upon Dry Vaccine.

(Duration of Exposure in each Experiment 30 minutes.)

No.	Maximum and Minimum limits of Temperature to which the Points were exposed. (Centigrade.)	The same in Fahrenheit degrees.	Introduced into Hot Chamber at	Temperature reached Minimum at	Temperature reached Maximum at	Removed at	Result.	
							Arm inoculated with Virgin Points.	Arm inoculated with heated Points.
1	57° – 59°	134·6° – 138·2°	1·10	1·19	1·21	1·49	2	2
2	60° – 63°	140° – 145·4°	12·9	12·12	12·15	12·42	3	3
3	63° – 66°	145·4° – 150·8°	12·47	12·49	12·51	1·20	2	3
4	67° – 70°	152·6° – 158°	4·40	4·43	4·44	5·12	2	1
5	69° – 74°	156·2° – 165·2°	4·42	4·47	4·51	5·17	3	3
6	75° – 80°	167° – 176°	11·34	11·51	11·58	12·21	3	3
7	85° – 90°	185° – 194°	12·47	12·54	12·56	1·24	Did not return.	
8	85° – 90°	„ „	1·51	2·7	2·11	2·37	3	0
9	90° – 95°	194° – 203°	4·15	4·28	4·33	4·58	2	0
10	90° – 95°	„ „	12·45	12·49	12·54	1·19	3	0

These results seem, at first sight, to differ from those obtained by Henry. The virulence of lymph was destroyed in his experiments at lower temperatures (49°–60° and 66°). The all but certain explanation of the difference is to be sought in the length of exposure. In the first instance (49°–60°), the vaccine was heated during four hours, in the second (66°), for two hours, while in the present series the exposure never lasted more than 30 minutes. The probability of this explanation is enhanced by the fact which has been noticed more than once, and recently confirmed by Roberts (Studies on Biogenesis, *Philos. Trans.*, 1874, part II.), that the destruction of the germs of septic microzymes by heat may be adequately accomplished, either by brief exposure to high temperatures, or by more prolonged exposure to lower ones; in short that degree of heat and length of exposure are mutually compensatory.

Davaine's researches on the effect of heat in destroying the activity of charbon virus.

In connexion with this part of the subject, Davaine's researches* on the effect of heat in destroying the infective power of the virus of *charbon* (malignant pustule) are deserving of notice. He has ascertained that the guinea-pig is peculiarly susceptible (much more so than, *e.g.*, the rabbit) to the action of this virus, when taken from a bovine animal suffering from the disease. $\frac{1}{1000}$ or even $\frac{1}{1000000}$ of a drop of blood from such an animal, when introduced into the subcutaneous areolar tissue of a guinea-pig, causes the speedy death of the latter, without any signs of local irritation. Such fractional doses are obtained by diluting a drop of blood with a known volume of water.

The virus after exposure to heat was invariably tested by inoculation into guinea-pigs. The following is a brief summary of the results:—

Exposure of the virulent blood diluted with an enormous excess of distilled water to a temperature of
- 55° C. disinfects it in 5 minutes.
- 48° C. „ 15 minutes.
- 50° C. „ 10 minutes.

When the blood is not diluted, its complete disinfection requires an exposure to 51° C. for 15 minutes. If the blood be previously dried

* *Comptes Rendus*, 29 September 1873.

over calcium chloride, and then heated to 100° C. for five minutes, its virulence is found not to be impaired.

These results confirm the statement already made that degree of heat and length of exposure are mutually compensatory. Further, they draw attention to the fact that differences in the physical condition of the virus,—in the nature of the medium in which its particles are suspended,—alter its susceptibility to disinfection by heat in a very striking way.

III. Experiments with the Virus of Infective Inflammation.

Virus of infective inflammation compared with the specific contagia.

The points of resemblance and difference between the virus of infective inflammation in rodents and the specific contagia of cow-pox and glanders have already been alluded to. The only essential difference between them was seen to be that whereas the latter cannot, by any means at present known to us, be generated anew, the former can be produced at will by introducing inflammatory products of any sort, or even chemical irritants, into the peritoneal cavity of a healthy animal, and employing the exudation-liquid resulting from the peritonitis for the inoculation of other animals. The pathology of the disorder has been fully discussed in the Medico-Chirurgical Transactions for 1873; it will not be necessary, therefore, to give any detailed account of it in this place. Some particulars, however, concerning the mode in which the virus was prepared, the effects to which it gave rise, and the method employed in testing the action of disinfectants upon it, are needed by way of introduction to the tabular summary of the experiments themselves.

Sources from which it was derived.

The virus was invariably derived from the peritoneal cavity of guinea-pigs which had succumbed to infective peritonitis. This peritonitis was sometimes primary, sometimes secondary; when primary, it was excited by the introduction of putrid pus, or of exudations from dogs which had died of artificial septicæmia, or of peritoneal exudation from other guinea-pigs, into the abdominal cavity; when secondary, it was a result of the subcutaneous inoculation of infective products derived from other guinea-pigs. The material employed had thus passed, now through one, now through several generations of animals; and though, as is well known, the virulence of the latter is much more intense than that of the former, it was not observed that there was any difference between them as regards their susceptibility to the action of disinfectants.

Its physical and chemical characters.

The physical and chemical characters of the virus were not always the same; it was commonly pale and viscid, occasionally sanguinolent and watery. It was always crowded with microzymes in the form of spheroids, dumb-bells, and necklaces; few or no rod-like bacteria were observed; and none of the organisms exhibited movements of translation. Notwithstanding the usually viscid and tenacious character of the material, it was found to contain but little solid matter. An analysis performed by Mr. Duguid shewed its sp. gr. to be 1019·3; when dried at 100° C. it left 5·0118 per cent. of solid residue, and this, on incineration, yielded ·793 per cent. of ash. In reaction it was always neutral or feebly alkaline.

Method of experimentation.

The degree of dilution of the virus employed varied within considerable limits; the amount of viscid exudation was sometimes so small that in order to obtain sufficient material for a series of inoculations it was necessary to wash out the peritoneal cavity with saline solution, and to add the washings to the unmixed liquid. The dose inoculated, though always small, was also not invariably the same. No surer proof of the genuine virulence of the liquid can be given than this, that whatever the dose, or the degree of dilution (within very wide limits), it either produced

its full specific effect, or no effect at all. It is right to add, however, that in each individual series of experiments, virus from the same source, diluted to the same extent, and in exactly the same dose, was injected into each of the animals. Further, that in every series the virulence of the unmodified liquid was established by a control experiment.

Guinea-pigs were employed in preference to rabbits for several reasons. A number of experiments made on rabbits turned out to be valueless owing to the very capricious and uncertain tenure on which these rodents hold their life. Some die suddenly without apparent cause; others survive the inoculation of liquids which prove rapidly fatal to their fellows; and the accidental death or survival of any one animal out of a series vitiates the result of the series as a whole. Again, the rabbits which succumb do not exhibit very definite structural lesions, so that it is often impossible to say whether a given animal has died in consequence of inoculation, or from some collateral and unknown cause. Guinea-pigs are more hardy; they do not commonly die without appreciable cause; and the inoculation of virulent liquids produces in them tolerably definite and constant structural alterations.

Lesions resulting from successful inoculation.

The lesions resulting from the injection of minute quantities of the above-described virus into the subcutaneous areolar tissue of the guinea-pig are never co-extensive with the tract of tissue presumably infiltrated with the liquid introduced; they either spread far beyond its limits, or else involve secondarily the great serous cavities. The appearances noticed may be roughly grouped under one or other of the following heads:—

1. The subcutaneous areolar tissue over a very large portion of the body is infiltrated with a thin, reddish, fetid liquid, swarming with microzymes; the skin is thus detached from the underlying parts and may become necrosed; the muscles are often discoloured and friable, looking as if macerated. Internal inflammations are absent.

2*a*. With a variable, though never very considerable, degree of local inflammation, there are all the signs of peritonitis; the intestines more or less glued together, the liver smeared with yellowish lymph, perhaps adherent to the diaphragm. A quantity, usually small, of viscid exudation, crowded with microzymes, occupies the most dependent part of the abdominal cavity.

2*b*. In addition to the peritonitis, similar marks of inflammation are seen in one or both pleuræ, and in the pericardium.

No very definite conclusions were arrived at concerning the immediate cause by which the occurrence of one set of appearances rather than of another was determined. One point stood out clearly, viz., that the difference in degree and character of the inflammatory changes was associated with some peculiarity of the material inoculated, and not with any idiosyncrasy of the animals. Virus from the same source always caused appearances of the same kind; and the existence of very extensive cellulitis was always found to coincide with the absence of serous inflammations. When the serous membranes were involved, the peritoneum was always the first to suffer; the pleurisy and pericarditis being always subsequent in the order of their evolution.

Tabular view of experiments performed.

The following table gives a summary view of the results obtained by allowing the four disinfectants to act on the virus. The length of time during which the virus was exposed to their influence varied from 30 minutes to three hours; this point appeared unimportant, since it was found that the action could be effectually completed within five minutes, provided that thorough mixture had been insured. The inoculations were invariably performed in the subcutaneous tissue on one side of the body; the point of a Pravaz's syringe being pushed through the skin half an inch from the spinous processes of the vertebræ, and passed downwards for about an inch.

Series.	No. of Animal.	Weight of Animal in grammes.	Date of Inoculation.	Material inoculated.	Dose.	Proportion of disinfectant Agent in the inoculated Material.	Interval of Time between Inoculation and Death.	Post-mortem Appearances, and Remarks.
I.	1	415	October 23	Virus diluted with its own volume of $\frac{1}{2}$ per cent. saline solution. The virus was freshly taken from the abdomen of a guinea-pig which died after the introduction of 3 minims of Cohn's solution, swarming with microzymes, into the peritoneal cavity; double pleurisy and pericarditis were found associated with the peritonitis. The exudation-liquid was yellowish and viscid, and full of microzymes.	4 m	0	36 hours	No local changes at site of inoculation visible to the naked eye. Peritoneal cavity contained a small quantity of viscid, yellowish exudation, crammed with organisms. Both surfaces of liver, under surface of diaphragm, and spleen, smeared with flaky lymph. No pleurisy or pericarditis.
	2	385	Do.	Same virus mixed with equal volume of 4 per cent. solution of carbolic acid.	4 m	2 per cent. carbolic acid.	- - -	No symptoms. Quite healthy on November 14.
	3	409	Do.	Same virus mixed with equal volume of 2 per cent. solution of carbolic acid.	4 m	1 per cent. carbolic acid.	- - -	No symptoms. Used for another experiment on January 16.
II.	4	428	February 2	Virus mixed with equal volume of saline solution. The virus was taken from the abdomen of a guinea-pig which died of peritonitis, caused by the introduction of putrid pus into its peritoneal cavity. It had been kept in a sealed tube in the laboratory (at a temperature of 60° – 65° F.) for several days.	5 m	0	- - -	None of the animals in this series showed any symptom of illness. The inoculated material was putrid. The animals were all employed again in other experiments, an opportunity being thus afforded of ascertaining that the present inoculation had left no visible traces.

Series.	No. of Animal.	Weight of Animal in grammes.	Date of Inoculation.	Material inoculated.	Dose.	Proportion of disinfectant Agent in the inoculated Material.	Interval of Time between Inoculation and Death.	Post-mortem Appearances, and Remarks.
II.	5	388	February 2	Same virus mixed with equal volume of 2 per cent. solution of carbolic acid.	5 m	1 per cent. carbolic acid.	- - -	No effect.
	6	390	Do.	Same virus mixed with equal volume of 1 per cent. solution of carbolic acid.	5 m	·5 per cent. carbolic acid.	- - -	No effect.
III.	7	596	February 9	Virus mixed with equal volume of saline solution. The material was a sanguinolent exudation from the peritoneum of a guinea-pig; the peritonitis had been caused by injection of similar exudation from another guinea-pig into the abdominal cavity. Had been kept in a sealed tube, embedded in ice, for two days.	5 m	0	24 hours	Succumbed to an acute cellulitis of great intensity. The skin was detached from the underlying tissues over the greater part of the thorax and abdomen by a thin, fetid, sanguinolent liquid, crowded with organisms. The abdominal muscles were pale, sodden, and friable. No signs of inflammation in the serous cavities.
	8	573	Do.	Same virus mixed with equal volume of 2 per cent. solution of carbolic acid.	5 m	1 per cent. carbolic acid.	- - -	No symptoms. Used again on March 2. It was then observed that the site of the present inoculation was marked by a small patch of thickening, about the size of a split pea.
	9	512	Do.	Same virus mixed with an equal volume of 1 per cent. solution of carbolic acid.	5 m	·5 per cent. carbolic acid.	40 hours	Same appearances as in 7. Moreover, the parietal layer of peritoneum was intensely injected, and studded with minute extravasations.

Series.	No. of Animal.	Weight of Animal in grammes.	Date of Inoculation.	Material inoculated.	Dose.	Proportion of disinfectant Agent in the inoculated Material.	Interval of Time between Inoculation and Death.	Post-mortem Appearances, and Remarks.
IV.	10	343	March 4	Virus mixed with an equal volume of saline solution. The virus was a viscid, pale liquid from the abdomen of a guinea-pig which died of infective peritonitis in 18 hours. The peritonitis was set up by the injection into the peritoneal cavity of two drops of a sanguinolent exudation from the belly of a dog which succumbed in seven hours to the most acute form of septicæmia. This had been caused by injection into its veins of an excessively virulent exudation procured by transmission through a series of guinea-pigs.	4 m	0	Killed on March 16	At site of inoculation an abscess as big as a cherry, filled with curdy pus; lymphatic glands in the neighbourhood of the scapula considerably swollen. Secondary deposit in one lung.
	11	375	Do.	Same virus mixed with an equal volume of 2 per cent. solution of carbolic acid.	4 m	1 per cent. carbolic acid.	- - -	No effect.
	12	393	Do.	Same virus mixed with an equal quantity of 1 per cent. solution of carbolic acid.	4 m	·5 per cent. carbolic acid.	18 hours	Slight ecchymosis at site of puncture; no cellulitis. Scanty, colourless, very viscid exudation in peritoneal cavity, crowded with organisms. No flakes of lymph. No pleurisy or pericarditis.

Series.	No. of Animal.	Weight of Animal in grammes.	Date of Inoculation.	Material inoculated.	Dose.	Proportion of disinfectant Agent in the inoculated Material.	Interval of Time between Inoculation and Death.	Post-mortem Appearances, and Remarks.
V.	13 Rabbit.	1,387	November 26	Virus mixed with equal parts of saline solution. Virus taken from peritoneum of guinea-pig, No. 31. Had been preserved in ice (in a sealed tube) for 16 days.	$2\frac{1}{2}$ m	0	48 hours	Subcutaneous tissue at site of inoculation slightly œdematous, and paler than surrounding parts. Some minute petechiæ on peritoneal covering of intestines. No other lesion observed.
	14 Rabbit.	1,004	Do.	Same virus mixed with equal parts of 2 per cent. solution of carbolic acid.	$2\frac{1}{2}$ m	1 per cent. carbolic acid.	- - -	In excellent health on January 20, when it was used for another experiment; no signs of present inoculation to be seen.
VI.	15	549	November 17	Virus mixed with equal quantity of saline solution. Virus derived from peritoneum of guinea-pig, No. 27. Had been kept in a sealed tube, in the laboratory, for 13 days.	$2\frac{1}{2}$ m	0	- - -	In perfect health on Jannary 16. The virus, kept during 13 days in a sealed tube, appears to have lost its infective power.
	16	462	Do.	Virus mixed with equal volume of solution of sulphur dioxide.	$2\frac{1}{2}$ m	·736 per cent. SO_2	- - -	No symptoms. Used again on January 16.
	17	371	Do.	Ditto - - -	$2\frac{1}{2}$ m	·2453 per cent. SO_2	- - -	No symptoms. Used again on January 16.
VII.	18	486	February 9	Same virus as that used for inoculating No. 7 (see *ante*), mixed with equal volume of saline solution.	5 m	0	24 hours	Same appearances as in No. 7.
	19	587	Do.	Same virus mixed with equal volume of solution of sulphur dioxide.	5 m	2·9 per cent. SO_2	- - -	Used again on March 2. No symptoms.
	20	380	Do.	Ditto - - -	5 m	·58 per cent. SO_2	40 hours	Diffuse cellulitis, as in No. 7.

Series.	No. of Animal.	Weight of Animal in grammes.	Date of Inoculation.	Material inoculated.	Dose.	Proportion of disinfectant Agent in the inoculated Material.	Interval of Time between Inoculation and Death.	Post-mortem Appearances, and Remarks.
VIII.	21	299	November 14	Virus mixed with equal volume of saline solution. Taken from peritoneal cavity of guinea-pig No 30. Pale, viscid, neutral. Not fetid.	$2\frac{1}{2}$ m	0	48 hours	Hardly a trace at site of inoculation. Scanty, colourless, very viscid exudation in abdominal cavity, crowded with microzymes. No pleurisy or pericarditis.
	22	560	Do.	Same virus mixed with equal volume of chlorine solution. The mixture was distinctly acid, and contained free Cl., as shewn by iodide of potassium and starch.	$2\frac{1}{2}$ m	·1563 per cent. Cl.	- - -	No symptoms. Died on December 12, after sudden onset of severe cold. No trace of inoculation, or of its specific effects, to be seen. No serous inflammation.
	23	385	Do.	Ditto - - -	$2\frac{1}{2}$ m	·07815 per cent. Cl.	- - -	No symptoms. Used again on January 16.
IX.	24	805	February 16	Virus, one part; saline solution, two parts. Same material as that with which No. 7 was inoculated. Had been kept in a sealed tube (in ice) for nine days.	5 m	0	36 hours	Same appearances as in No. 7.
	25	388	Do.	Virus, one part; saline solution, one part; solution of potassic permanganate, one part -	5 m	·1 per cent. of permanganate.	- - -	No symptoms.
	26	810	Do.	Ditto - - -	5 m	·05 per cent of permanganate.	- - -	No symptoms.

It appears, as a result of the above experiments, that carbolic acid in the proportion of 1 per cent. or more, chlorine in that of ·078 per cent. or more, sulphur dioxide in that of 2·9 per cent. or more, and permanganate in that of ·05 per cent. or more, are capable of so modifying the virus as to deprive it of all infective power. It should be noted that in the solutions disinfected with chlorine, the presence of this gas in a free state was always shewn by potassic iodide and starch after mixing had been completed; and that the liquids containing SO_2 were decidedly acid in reaction. Further experiments with the same virus will be described in the concluding section of the report.

The researches of Davaine* upon the action of disinfectants on the virus of *charbon*, and those of Rosenbach† on the influence of carbolic acid in preventing pyæmic and putrid infection, furnish results which may be usefully compared with the above.

Davaine on the action of disinfectants on charbon virus.

Davaine employed the blood of an animal suffering from malignant pustule, diluted with 100 parts of water, for inoculating guinea-pigs, which are peculiarly susceptible to the action of this virus (*Cf.* p. 14). The virulent liquid was mixed with a solution of the disinfectant, and allowed to stand from 30 minutes to an hour before being inoculated. Death resulted from the hypodermic injection of minute quantities of the liquid, when its activity had not been destroyed, in from one to four days; sometimes, though rarely, the guinea-pigs survived till the eighth day. These points indicate a very considerable degree of resemblance between the effects of the *charbon* virus and those produced by the infective products employed in the present investigation.

A number of disinfectants were tested; singularly enough, chlorine and sulphur dioxide were not included in the list. The best results were furnished by iodine, which destroyed the infective property of the liquid in the proportion of ·0083 per cent. Chromic and sulphuric acid, though inferior to iodine, stood higher than potassic permanganate and carbolic acid. When the permanganate was added to the virus in the proportion of ·1, ·08, ·0333, ·02, per cent., inoculation was followed by recovery; ·0166 per cent. was found ineffectual. Carbolic acid, when present in the proportion of 1 per cent. or more, destroyed the virulence of the liquid; ·5 per cent. failed to do so; one experiment with virus containing ·75 per cent. of the acid ended in the recovery of the animal.

These results are in obvious agreement with those derived from the experiments performed with the virus of infective inflammation, and differ widely from those furnished by vaccine. The probable explanation of this discrepancy will be considered in the concluding section of the report.

Rosenbach's experiments on the disinfectant power of carbolic acid.

Rosenbach's inquiries were limited to the action of carbolic acid on pus. They deserve mention in this place chiefly because the method employed to determine the effect of the acid was that on which we have insisted as the only right one: the disinfected material being inoculated on a living animal, and the result compared with that due to the inoculation of the same material prior to the admixture of any disinfectant.

Three varieties of pus were employed for inoculation. The first series of experiments was conducted with pus which had undergone decomposition in the body before its removal; the second with pus which was perfectly fresh when removed from the body, but which

* *Comptes Rendus*, 13 October 1873.

† *Untersuchungen über den Einfluss der Carbolsäure gegen das Zustandekommen der päymischen und putriden Infektion bei Thieren.* Göttingen, 1872.

had been subsequently allowed to putrefy; the third series comprised inoculations with fresh (non-putrid) pus drawn from acute abscesses. The animals inoculated were rabbits and dogs, and the material was always introduced into the subcutaneous tissue in comparatively large quantities (5—15 c. c.). The infective character of the liquid manifested itself by causing diffuse phlegmonous inflammation, spreading from the inoculated spot, and proving rapidly fatal; when this primary effect was less intense the animals either recovered, or succumbed to secondary mischief of a pyæmic kind. The appearances were by no means constant; and this lack of uniformity is intelligible enough when we consider the very uncertain character of the materials employed for inoculation.

The presence of 5 per cent. or more of pure carbolic acid in the inoculated material rendered it harmless; 1 per cent. was uncertain in its effect; smaller quantities were always ineffectual. The acid was found to be less powerful in its effect on pus which had been allowed to putrefy outside the body, than on pus which was already fetid when discharged. These results, though not opposed to our own, are vitiated—as regards the purpose in hand—partly by the very uncertain nature of the material used, partly by the indiscriminate employment of animals so different in their susceptibility as dogs and rabbits, and finally by the capricious variety of the symptoms and morbid changes produced.

IV. Experiments with the Virus of Glanders.

Although the following experiments performed with the infective material of glanders are neither so numerous, nor, with one exception, so convincing as those already described, it has been thought desirable to place them on record, partly because no similar trials have hitherto been made; partly because any observed facts relating to a disease at once profoundly interesting, and, considering its frequency, so little studied, have in themselves a positive worth apart from the immediate object for which they have been sought.

Nature and properties of the virus of glanders.

There are two more particular reasons why the virus of glanders should commend itself to the notice of those engaged on such an inquiry as the present one. In the first place, it is one of the few acute specific diseases to which man is liable in common with certain of the lower animals. In this respect it stands upon a different footing from cattle-plague or ovine variola. Ever since the disease was recognised in the human subject by Elliotson in this country, by Rayer in France, similar cases have annually been noticed and put on record. Secondly, the nature of the infective material has been subjected by Chauveau and others to an investigation similar in method, and furnishing similar results, to that pursued in reference to the contagia of cow-pox, small-pox, and variola ovina. It has been proved that the contagious principle of glanders is neither soluble, nor diffusible, nor volatile; and that by inference it must consist of minute solid particles. The nature of these particles in this case, as in the others, is still open to question. There is no proof that they are capable of being generated otherwise than in a previously infected organism; and there is abundant evidence to prove that when introduced in the most minute quantity into a suitable medium, they undergo multiplication to an enormous extent, and with enormous rapidity. The morbid product of the glanderous process has thus the distinctive mark of a virus, and of a specific virus; specific, inasmuch as it cannot be produced *de novo* by any means now known to us, and

is not inoculable on all animals indiscriminately; the horse, the ass, and the human subject being readily susceptible to its influence, while it does not seem to produce any effect upon the rabbit.

Preparation of the virulent liquid.

The virulent material employed in the first series of inoculations was prepared as follows. The nodules of infective pneumonia in the lung of a horse labouring under acute glanders, and which had just been killed, were cut out with scissors and bruised in a mortar with the addition of a small quantity of half per cent. saline solution. The nodules varied in size from a pea to a walnut; they were of a yellowish-grey tint, firm, and somewhat elastic. The creamy liquid, full of shreds of tissue, which was thus obtained, was filtered through a double fold of muslin. The filtered material was of a bright red colour owing to admixture of blood, neutral to test-paper, and coagulable by heat and nitric acid. Under the microscope it was seen to contain a vast number of shrunken and distorted red blood-corpuscles, epithelium cells, and other tissue-elements; besides these, a multitude of extremely minute, highly refracting, motionless spheroids, but no locomotive microzymes. When the liquid was allowed to stand, an abundant sediment of a dirty red colour formed at the bottom of the glass; it consisted of the corpuscular elements enumerated above.

Method of experimentation adopted in Series A.

It was anticipated that the local phenomena produced by the inoculation of this liquid would manifest themselves with sufficient distinctness before the general invasion of constitutional disturbance, to enable a number of inoculations to be simultaneously carried out on the same animal. In an inquiry which involved repeated inoculations, and which could only be conducted on large animals, such as horses or donkeys, this was the only practicable course. The issue of the first series of experiments showed, however, that this method, though yielding results of a considerable degree of probability, was nevertheless open to objection on the score of uncertainty.

The infective liquid described above was divided into two equal parts. One of these was put aside (I). The other was washed with half per cent. saline solution so as to separate its solid constituents, as far as possible, from the soluble matters with which they were mingled. The washing was carried out as follows: a large excess of saline solution having been added to the liquid, the two were shaken up together, and the mixture set aside in several tall narrow test-tubes; after a couple of hours the supernatant liquid was removed from each tube by a siphon, without disturbing the sediment. Fresh saline solution was then poured into each tube and the process repeated. This was done six times, and the resulting sediments were then collected in a single tube. They formed a flocculent stratum of a dirty-white colour, the supernatant liquid being only slightly turbid; heat and nitric acid caused a doubtful increase of this turbidity, but threw down no precipitate. This almost aqueous liquid, holding a number of whitish flocculi in suspension, will be denominated (II).

It had already been shewn by Chauveau, though for another purpose altogether, that the solid elements of a mixture holding the infective material of glanders in suspension could be separated by repeated washing and decantation from the soluble compounds with which they were associated, and that the washed residue retained its infective power. The operation was meant in the present instance to furnish a virulent liquid containing a minimum of such organic and mineral constituents as might be expected to influence the action of disinfectant agents; in short, to replace the complex medium in which the contagium was suspended, as thoroughly as might be, by saline solution.

The portion of virulent liquid marked (I) was then distributed into five

App. No. 6.

On Disinfectants, by Dr. Baxter.

Disinfectants employed in this series of inoculations.

tubes, each of which was made to contain 2 c.c. of it. The following additions were then made to the contents of the several tubes:—

1. To this was added an equal volume of saline solution.
2. Was mixed with 2 c.c. of a freshly made two per cent. solution of carbolic acid.
3. Mixed with 2 c.c. of ·1 per cent. solution of potassic permanganate.
4. Mixed with 2 c.c. of solution of sulphur dioxide (containing 3·88 per cent. of the gas).
5. Mixed with 2 c.c. of a weaker solution of sulphur dioxide (containing ·518 per cent).

The permanganate in 3 was quickly decolorized; the two solutions containing sulphur dioxide were instantly blackened. 1 and 2 shewed no change of colour.

2 c.c. of the portion of liquid marked (II) were then introduced into each of three tubes.

The following additions were made:—

6. To this 2 c.c. of saline solution were added.
7. Mixed with an equal volume of 2 per cent. solution of carbolic acid.
8. Mixed with an equal volume of ·1 per cent. solution of potassic permanganate.

The eight mixtures thus prepared were then introduced into tubes drawn out at each end into capillary extremities, and sealed up. The tubes were preserved in ice. The following table gives at a glance the proportion of disinfectant contained in each of the liquids:—

1.	Not washed.	No disinfectant.
2.	Do.	Carbolic acid, 1 per cent.
3.	Do.	Potassic permanganate, ·05 per cent.
4.	Do.	Sulphur dioxide, 1·94 per cent.
5.	Do.	do. ·259 per cent.
6.	Washed sediment.	No disinfectant.
7.	Do.	Carbolic acid, 1 per cent.
8.	Do.	Potassic permanganate, ·05 per cent.

Series A.

On January 11, 24 hours after the above liquids had been prepared, an old healthy male donkey (hereafter to be known as M) was inoculated in eight places. Four patches of skin had previously been shaved on each side of the trunk; they were nearly equidistant from one another, the first of each series being on the shoulder, the last close to the thigh. The animal had been kept under observation for eight days, and his temperature had been taken daily in the rectum. The mean of these eight observations was 100·2° F.

The inoculations were performed by plunging the nozzle of a hypodermic syringe into the subcutaneous areolar tissue, and injecting 10 minims of the liquid. After each inoculation, the syringe was thoroughly washed with saturated solution of carbolic acid, and then with water. Each of the eight patches accordingly received 10 minims of one of the eight liquids enumerated above. The injection did not seem to cause the animal any annoyance, except in the case of the solutions containing sulphur dioxide, which were decidedly acid.*

* The inoculations were performed and the symptoms observed by Mr. Duguid, veterinary surgeon to the Brown Institution, to whose familiarity with the disease, and cordial co-operation, this set of experiments owes whatever value it may be found to possess.

Record of symptoms.

The following is a brief record of the progress of the case. The numbers correspond to those of the liquids introduced :—

Jan. 12.	T—101·3° F.	Some thickening to be felt in all of the inoculated spots.
„ 13.	T—104·3.	Patch 1 discoloured, hot and tender.
„ 14.	T—103·2.	
„ 15.	T—104·8.	Swelling extending downwards to the knee, forwards to the sternum.
„ 16.	T—104.	
„ 17.	T—104·2.	
„ 18.	T—104·6.	Small bullæ have made their appearance over patch 1.
„ 19.	T—105.	Copious discharge from right nostril. Small farcy-bud on right upper lip. Chain of nodules extending along course of jugular vein from patch 1. Other nodules can be felt elsewhere under the skin, chiefly, but not exclusively, in the vicinity of the inoculated patches.
„ 20.	T—104.	Refuses food. Breathing laboured and stertorous.
„ 21.		Farcy-buds scattered about the body. Scrotum and testes much swollen.
„ 22.		Found dead this morning. Post-mortem examination made several hours after death. The following is a brief summary of its results :—

Post-mortem appearances.

The skin over patch (1) was black, and seemed on the point of sloughing. The patch of skin corresponding to (6) was distinctly indurated, and the neighbouring lymphatics were corded. The remaining six patches were for the most part free from any decided change, except a little subcutaneous thickening. But in the immediate neighbourhood of almost all of them one or more subcutaneous nodules could be felt. Similar nodules, however, were irregularly distributed under the skin in parts remote from the site of any inoculation. When the skin was removed, the tissues under (1) were found to be gangrenous; the entire thickness of the muscles having been converted into a putrid mass of reddish-yellow material, breaking down at its centre into a fetid ichor. The site of (6) was occupied by a large deposit of caseous material softening at its centre; the areolar tissue round it was dotted with extravasations. Yellowish nodules and patches of capillary ecchymosis were found in the immediate vicinity of every one of the inoculated spots; but similar nodules and patches existed all over the body; the utmost one could say was that the nodules were more closely aggregated and more numerous near the site of the inoculations than elsewhere. The subpleural and subpericardial tissue was everywhere studded with minute petechiæ. Nodules of infective pneumonia were scattered throughout both lungs, which were intensely œdematous. The trachea and bronchi were full of frothy secretion; on splitting open the nostrils, the mucous membrane was found congested in patches; a few nodules resembling miliary tubercles were seen in the submucous tissue; no ulceration had as yet taken place. Both testicles were much swollen, and contained secondary deposits; the left one was almost black from intense congestion.

These appearances were amply sufficient to shew that the animal had succumbed to the most virulent form of acute glanders, and that the

inoculated liquids 1 and 6 had started the disease. But the invasion of constitutional infection had been too rapid and violent to allow the local phenomena consequent upon inoculation to develope themselves freely; the primary and the secondary lesions had manifested themselves almost simultaneously, and there was an obvious difficulty in deciding to which of the two categories any particular subcutaneous lesion ought to be assigned. In the first place, however, there was a very marked difference, both qualitative and quantitative, between the changes observed in (1) and (6), and those detected in the remaining patches; secondly, the nodules and hæmorrhagic maculæ in these latter patches were identical with others situated in parts far removed from the site of any inoculation. For these reasons, it seemed highly probable that the lesions observed in all the patches except (1) and (6) were really part of the secondary process, products of constitutional infection; and their presence in greater number in the neighbourhood of the inoculated spots was attributed to the local irritation caused by the chemical nature of the materials injected, just as an exanthem is more abundantly localized in the neighbourhood of a wound or other focus of irritation than elsewhere.

Inferences from the experiment.

To sum up, the virulent liquid *appears* to have been deprived of its infective power by the addition of 1 per cent. of carbolic acid, ·05 per cent. of potassic permanganate, 1·94 per cent. and ·259 per cent. of sulphur dioxide; and, in these proportions, the disinfectant agents seem to have acted as effectually upon the unwashed as upon the washed virus.

Series B.

Method adopted in Series B.

In order to obtain results free from the possible objections to which those in series A are liable, it was resolved to inoculate only one place at a time, allowing a week to elapse after each inoculation; the absence of any rise of temperature or other untoward symptom during this interval affording sufficient proof of the harmless nature of the material inoculated. A large supply of virus was prepared, in the manner already described, from the infective nodules in the lungs of the last donkey. It was preserved in hermetically sealed glass tubes.

Experiment with carbolic acid.

A young, healthy, male donkey (N), was kept under observation for several days, and his mean temperature was ascertained to be 100° F. On January 25, 10 minims of the following mixture were injected into the subcutaneous areolar tissue over the left shoulder; virus diluted with an equal volume of a 4 per cent. solution of carbolic acid. The temperature rose on the third day after inoculation to 102° F., and the inoculated spot was hot and tender. On the ensuing day, however, the temperature had fallen to 100° F., where it remained; the tenderness and swelling gradually disappearing in the course of the next few days.

With sulphur dioxide.

On February 4, a second inoculation was performed on the right shoulder. The virus was mixed with its own volume of a solution of sulphur dioxide, containing 2·88 per cent. of the gas; the mixture was strongly acid, and of a blackish colour; 10 minims were injected. The acid liquid caused considerable swelling and tenderness, which took several days to subside. The temperature never rose at all.

With carbolic acid and chlorine.

A new donkey (old, male) having been obtained (O), the two animals were inoculated simultaneously on Febuary 11. N received 10 minims of a mixture of equal parts of the virus and 2 per cent. solution of carbolic acid; while O was inoculated with the same quantity of a mixture of equal parts of the virus and Chlorine solution (containing ·3266 per cent. of the gas).

The addition of carbolic acid turned the virulent liquid of a brighter red; its reaction continued neutral. Under the influence of chlorine,

its colour changed to a dirty bottle-green; the mixture being decidedly acid, and containing free chlorine (as shewn by potassic iodide and starch). The result of the two experiments is shewn in the following table:

N. (Normal Temperature, 100° F.	O. (Mean Temperature before Inoculation 100° F.)
Feb. 12. T.–103·2. Inoculated spot swollen, hot, tender, and slightly discoloured.	Feb. 12. T.–100·2. A small hard nodule can be felt at the site of inoculation. Not tender.
„ 13. T.–103. Swelling is extending.	„ 13. T.–100·4.
„ 14. T.–100·8.	„ 14. T.–99·8.
„ 15. T.–100·8. Swelling and tenderness are subsiding.	„ 15. T.–100·4.
„ 16. T.–100·4.	„ 16. T.–100·2. Nodule has disappeared.
„ 17. T.–100·3. Swelling has nearly disappeared.	„ 17. T.–99·8.
„ 18. T.–100·2.	„ 18. T.–99·8.

The rise of temperature and local disturbance which occurred in N. are phenomena difficult of explanation. For three days after the animal had been inoculated, it was believed that the inoculation had proved effectual; but the untoward symptoms passed off as rapidly as they had set in. On February 18, N. and O. were again inoculated; but it was noticed that the virulent liquid had a decidedly putrid odour, very different from the faint animal aroma which it had previously given off. The tubes, owing to a deficiency in the supply of ice, had been kept in the open air, the weather being very cold. A sudden thaw, which lasted for two or three days, had evidently allowed their contents to undergo decomposition. No result having been noticed to follow the two inoculations on February 18th, 10 minims of unmixed virus were injected into N. on the 23rd; no symptoms followed, with the exception of slight local tenderness.

Putrefaction of virulent liquid.

The control experiment having thus proved a failure, any deductions from the experiments belonging to this series must necessarily rest upon the assumption that up to and including February 12, the virulent liquid had retained its infective properties. In favour of this assumption we have the facts that the liquid, up to that date, had been exposed to a very low temperature and had shewn no sign of putrefactive change;* also that it gave rise to anomalous, but marked symptoms after its admixture with 1 per cent. of carbolic acid. Still, the following results, however probable, are not absolutely certain; namely, that the presence of 2 per cent. of carbolic acid, of 1·44 per cent. of sulphur dioxide, of ·1633 per cent. of chlorine deprived the virulent liquid of its specific properties; and that although the presence of 1 per cent. of carbolic acid annulled its specific infective power, it allowed it to produce local and general symptoms of a grave kind.

Inferences from this series of inoculations.

Series C.

A fourth donkey (P) having been obtained, whose fore-leg was irremediably damaged by an accident, but which was otherwise in good health, it was resolved to perform three inoculations at the same time, one on each of the three animals. Fresh material having been prepared

Method followed in Series C.

* It was incidentally noticed in the course of the present enquiry, that putrefactive change, occurring in the virus of vaccine, in that of experimental septicæmia, and in that of glanders, appeared invariably to destroy their specific infective power.

App. No. 6.

On Disinfectants, by Dr. Baxter.

in the usual way from the pulmonary nodules of a horse suffering from glanders, the following experiment was carried out on March 4. N. received 10 minims of a mixture of the virus with an equal volume of 4 per cent. solution of carbolic acid; O, a similar quantity of a mixture of the virus with an equal volume of solution of sulphur dioxide (containing ·8 per cent. of the gas); P, 10 minims of a mixture of equal parts of virus and 1 per cent. solution of carbolic acid. The mixture containing SO_2 was strongly acid; the other two were neutral. The result of the three inoculations is given in the following table:

Record of symptoms.

N.	O.	P. (Mean Temperature before Inoculation 100° F.)
March 5. T–100. Small nodule, not tender, at site of injection.	March 5. T.–99·8. Slight thickening felt at inoculated spot.	March 5. T–100°. Inoculated spot slightly swollen and tender.
„ 6. T–100·2.	„ 6. T–100.	„ 6. T–100·2.
„ 7. T–100·2.	„ 7. T–100.	„ 7. T–102·6. Very tender.
„ 8. T–100·4. Nodule has disappeared.	„ 8. T–100·4.	„ 8. T–104·6. Skin hot and discoloured over injected patch.
No further symptoms or rise of temperature.	No further symptoms or rise of temperature.	„ 9. T–104·8. Animal appears decidedly ill.
		„ 10. T–103·8.
		„ 11. T–103·2. Refuses food. Corded lymphatics round swollen patch.
		„ 12. T–103·6. Tenderness very great; swelling travelling down leg; farcy-buds appearing on the neck.
		„ 13. T–103.
		„ 14. T–103·2.
		„ 15. T–103. Discharge from nostrils. Breathing quick and laboured.
		„ 16. Found dead this morning.

Post-mortem Examination of P. on March 16.

Post-mortem appearances.

At the site of inoculation the skin is bound down to the deeper tissues by a patch of exudation, as large as a man's hand, studded with capillary hæmorrhages. The areolar tissue all down the corresponding leg is infiltrated with a serous liquid; distended and knotty lymphatics radiate from the affected spot. On cutting into the underlying muscles, a large ragged cavity is laid open, full of yellowish curdy pus; round this are scattered smaller deposits of a similar kind varying in size from a pea to a walnut. On stripping off the skin at a point about two feet away from the inoculated spot, a large yellowish nodule is discovered in the subcutaneous tissue; around it are innumerable capillary extravasations. (This lesion was situated at the point where a second inoculation would have been performed had the method employed in series A. been adopted in the present instance, and it might then have been attributed to a primary local infection.) A few similar deposits were noticed elsewhere. There was an absence of putridity about the primary lesion which contrasted markedly with the appearances in M.

On opening the thorax, several patches of capillary extravasation were observed under the costal pleura. Both lungs were crowded with

yellowish nodules of infective pneumonia, varying in size from a pea to a pigeon's egg. They were all firm and somewhat elastic; when subpleural, they were surrounded by a zone of congestion, but the pleura over them retained its normal smoothness. Trachea and bronchi full of frothy secretion. The mucous membrane lining the nasal cavities was much reddened; no nodules were detected in it on a cursory inspection.

Results from Series C.

The result of the three experiments in this series is incontestable. The presence of 2 per cent. of carbolic acid, or of ·4 per cent. of sulphur dioxide sufficed to destroy the infective power of the virus employed, and the presence of ·5 per cent. of carbolic acid did not impair its virulence in the least.

V. Experiments with Septic Microzymes.

Relation of disinfectant power to certain other properties.

In the introductory part of the present report it was stated that much of what had been hitherto done by way of determining the relative efficacy of disinfectants was radically vitiated by the very loose meaning attached to the term. Numerous experiments have been made in order to ascertain the power of various agents to prevent or arrest catalytic, zymotic, and septic processes; and the results of such experiments have long been taken as a measure of comparative disinfectant power. Further, some authors fail even to distinguish between the destruction of the noxious products of putrefactive decomposition and that of the specific contagia. This last element of perplexity may, however, be summarily dismissed; the problem is obviously and wholly chemical; the nature of the liquid or volatile products whose hurtful influence is dreaded in any particular case, necessarily defining the nature of the agent required to decompose or to combine with them. But the former series of results is deserving of closer attention. For although their employment as a means of estimating the comparative power of various disinfectants depends on the implied assumption of some fundamental relationship between the mode in which such processes are propagated and that in which communicable diseases are spread, and although no such assumption can at present be regarded as sufficiently established to serve as a basis for deductive inference, yet it is clear that had no similarity been noticed between the effect of disinfectants on the processes above enumerated, and their utility in arresting the spread of contagious disease, the practical good sense of inquirers would soon have led them to retrace their steps and abandon a method of investigation yielding results in obvious contradiction to those of everyday experience. A method based—perhaps unconsciously—upon a hypothesis in which many of those who employed the method did not believe, must have owed its continued popularity to coincidences observed to hold good between the two sets of phenomena. This seems the most likely explanation of what wears, at first sight, the aspect of a paradox; viz., that the very persons who repudiate all belief in the parasitic theory of contagion, nevertheless continue to put faith in disinfectants whose claim to credit logically depends on the truth of some such theory.

These considerations appeared to furnish a motive for discussing the question by the light of the facts ascertained in the foregoing series of experiments. It seemed worth while to ascertain, if possible, whether any relation could be demonstrated between the strictly disinfectant properties of the substances under investigation, and their power to

influence catalytic, zymotic and putrefactive processes. Should the existence of some such relation turn out not to be wholly imaginary, it will tend, *pro tanto*, to support a particular view of contagion; though the acceptance of the connection need not of course entail the acceptance of the pathological theory.

Its relation to the power of checking or arresting catalytic change.

The first of the three processes, whose relation to disinfectants has been studied, is the peculiar catalytic change determined in certain compounds by a nitrogenous ferment, and seemingly independent of the presence of living organisms. The analogy between such catalytic processes and the phenomena of contagion and infection is most clearly present to the mind of those pathologists who attribute an infective power to all the albuminoid constituents of the diseased organism, a power depending entirely upon their molecular condition, and independent of the "vital" endowments of the corpuscular elements of the blood and tissues. The obscurity which shrouds the intimate nature of any such process is expressed rather than explained by the term "catalysis." That there exists a certain show of likeness between the two sets of phenomena it would be unfair to deny; and even those most firmly attached to the hypothesis never claim for it the authority of a demonstrated truth.

The following catalytic processes have been studied in relation to carbolic acid: the action of emulsin upon amygdalin, that of myrosin on the myronate of potash contained in black mustard-seed, that of emulsin upon salicin, that of saliva and diastase on starch, that of pepsin on albumen and fibrin.* It may briefly be said that the acid, unless present in very large proportions, is incapable of exercising any material influence on any of these processes except the last; and even the last is not very susceptible to its influence; for Zapolsky found it necessary to add 5 drops of the pure acid to 10 cubic centimètres of artificial gastric juice in order to arrest its solvent action on ·5 gramme of fibrin.

The relation of the remaining three disinfectants on our list to the above processes has not, so far as I know, been studied; nor is this of any moment; for the results obtained with carbolic acid are sufficient to prove that the phenomena of catalysis cannot furnish any analogies to disinfection, strictly so called.

Its relation to the power of checking or arresting fermentation.

We have next to consider the influence of disinfectants upon fermentations causally associated with the presence of organisms of the *Torula* kind. Of these, alcoholic fermentation is the familiar type. Many writers habitually place fermentations and putrefactions in the same group, and deal with them as essentially similar processes. From a chemical point of view, this may be justifiable. But it is not to the chemical results of the process, it is to the organic forms associated with the production of those results, that our attention has to be directed. One writer on disinfectants (Dr. Dougall, *loc. cit.*) has been at great pains to distinguish between what he calls the "antifermentative" and the "antiputrefactive" power of various agents, and to express their relation to each other numerically, the sum of the two constituting what he terms "total antiseptic power." The chief differences between the two sets of phenomena may be summarised as follows:—

1. Fermentations are associated with the presence of torulaceous organisms, putrefactions with that of bacteroid forms.

* Those desirous of fuller details are referred to the following authorities: *Zapolsky* (Hoppe-Seyler's *Med. Chem. Untersuchungen*, 1871); *Lemaire* (l'Acide Phénique); *Plugge* (Die Carbolsäure, *Pflüger's Archiv*, vol. X. 1872); *Crookes* (Report on Disinfectants, Cattle Plague Commission, 1866); *W. Buchholtz* (Die Einwirkung der Phenylsäure auf einige Gährungsprozesse. Inauguraldiss. Dorpat, 1866).

2. The former occur by preference in acid, the latter in neutral or alkaline media.

3. The germs needed to excite the former are abundantly present in air; those required for the latter are sparingly distributed through air, but abundant in water.

4. The chemical changes wrought by the former are much more rapid than those wrought by the latter.

5. The organisms connected with fermentation are more easily destroyed, or robbed of their reproductive power, than those associated with putrefaction.

It must, of course, be understood that this attempt to separate between the two groups of phenomena is entirely relative to the matter now in hand; it would be highly presumptuous to offer it as the solution of a many-sided problem which must one day be settled upon wider grounds.

The action of disinfectants on the organisms connected with fermentation need not detain us long. There is much evidence to show that fermentation is far more easily arrested than putrefaction; and that torulaceous germs are more susceptible to the action of heat (Roberts, Studies on Biogenesis, *Phil. Trans.*, 1874), and to that of chlorine and of potassic permanganate, than the germs of the *Schizomycetes*. Jüdell* has shown that the exposure of yeast to an atmosphere containing ·25 per cent. (by volume) of SO_2 for a variable number of hours destroys its zymotic properties. Manassein found $\frac{1}{16}$ per cent. of carbolic acid sufficient to deprive the spores of *Penicillium* of their germinating power. Experiments made by myself point in the same direction. It may fairly be concluded that the influence of disinfectants on such fungoid spores affords no measure of their action on contagia, since the former are very much more susceptible to adverse influences than the latter.

Its relation to the power of checking or arresting putrefaction.

The strictly antiseptic energy of disinfectants is undoubtedly that which has been most thoroughly investigated, and most frequently taken as a measure of their power to destroy contagion. A vast mass of experimental material on this subject has been accumulated by Angus Smith, Calvert, Crookes, Parkes, O'Nial, Dougall, and many others in this country, not to speak of countless researches made in France and Germany. The popularity of this method has been shown to depend, partly on a vague sense of resemblance between the spread of putrefaction and that of contagion; partly on a belief that specific contagia may be created *de novo* in putrefying matter; partly on coincidences empirically observed between the operation of disinfectants in the two sets of cases; partly on the difficulty of obtaining direct evidence of their value. Without committing ourselves to any opinion on the vexed question of the parasitic theory of contagion, it seems desirable to find out whether any quantitative relation between the antiseptic and the disinfectant power of our four agents can be shown to exist. It is needful to premise that the word "antiseptic" is here taken to mean "fatal to the growth and multiplication of septic microzymes." The nature of the connexion between microzymes and the chemical phenomena which coincide with their evolution is provisionally set aside. Whether putrefactive decomposition may occur as a result of purely chemical agencies, and without the intervention of bacteroid organisms, is a question foreign to the matter in hand. Hoppe-Seyler† has proved to his own satisfaction that it may. But the analogies of the contagia are with septic microzymes, not with processes of oxidation or deoxidation. Septic microzymes, like the contagia, multiply indefinitely when

* *Hoppe-Seyler's Untersuchungen*, 1868.

† *Med. Chem. Untersuchungen*, 1871. Uber Fäulnissprozesse und Desinfektion.

introduced, in all but infinitesimal proportions, into suitable media; so far the analogy is shared by the torulaceous ferment-organisms; on the other hand, septic microzymes, like contagia, thrive in alkaline or neutral media; and organisms morphologically identical with them have been shown to exist in many infective liquids.

True nature of the analogy between putrefaction and contagion.

Before describing the experiments, it is necessary to clear up a preliminary misconception which has been a source of endless confusion in the past. The antiseptic power of a given agent has usually been tested by adding it, in some known proportion, to a substance capable of serving as a nidus for the evolution of septic microzymes, and noting whether it succeeded or failed in preventing their appearance. Now there can be no question that small quantities, say of carbolic acid, are able to prevent the growth of microzymes in media otherwise favourable to them; that minute proportions of potassic permanganate or chlorine added to such media may so act upon the materials which are the pabulum for microzymes as to deprive them of their nutritive power. Thus, for example, $\frac{1}{8}$ per cent. of carbolic acid suffices to prevent the putrefaction of bread pulp, $\frac{1}{5}$ per cent. that of flesh-broth, and of milk.* Such proportions, as we have seen already, are destitute of disinfectant power; and all idea of a quantitative correlation would have to be abandoned, were this the only, or the correct method of investigation. The real question is this: what proportion of a given disinfectant, added to a liquid containing microzymes or their germs, will deprive these of their power to multiply when introduced into a medium hitherto barren, but endowed with all the conditions of fertility. The following was the method adopted in seeking an answer to this question.

Method employed for tracing a quantitative relation between antiseptic and disinfectant power.

A known proportion of the agent under investigation was added to a liquid teeming with septic microzymes. A test-solution, previously sterilised by heat, was then inoculated with a minute drop of the disinfected† liquid. If it continued barren, the successful destruction of the septic germs was proved; in the event of their incomplete destruction, the test-liquid was found crowded with their progeny. The septic microzymes were invariably cultivated in Cohn's solution,‡ modified by the omission of the calcium phosphate; this solution, as is well known, remains permanently limpid and barren after being boiled, if protected against accidental contamination; on the other hand, the introduction of the smallest quantity of septic microzymes, or of their germs, renders it turbid in 48 hours. The first experiment of the series will be fully described, as an illustration of the method of procedure; of the subsequent ones, the results only will be given.

I. *Action of Potassic Permanganate on Septic Microzymes.*

Experiments with potassic permanganate.

1. Six éprouvettes were charged with 1 c.c. each of Cohn's solution, swarming with microzymes. Each éprouvette then received 1 c.c. of one of the following six solutions of permanganate in distilled water: 1, 8 per cent.; 2, 6 per cent.; 3, 4 per cent.; 4, 2 per cent.; 5, 1 per cent; 6, ·5 per cent. The liquids in the six éprouvettes were

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* Plugge.

† In describing the following experiments, the terms "disinfected," "infective," &c. are, of course, used metaphorically.

‡ Its composition is as follows:

Ammonium tartrate, 2 grm.
Magnesium sulphate, Potassic phosphate } of each 1 grm.
Calcium phosphate, ·1 grm.
Distilled water, 200 c.c.

The calcium phosphate does not dissolve properly in the liquid, and interferes with its limpidity; it may be omitted without detriment.

thus made to contain 4, 3, 2, 1, ·5, and ·25 per cent. respectively of the disinfectant. They were set aside for some hours under a bell-jar. Eight fresh éprouvettes were in the meantime thoroughly roasted in the flame of a Bunsen burner. Into each of these 3 c.c. of boiling Cohn were introduced, and they were set aside to cool under cover. When cool the first six were inoculated with one drop each of the six disinfected solutions; the seventh was left without interference; the eighth was inoculated with a drop of the original liquid which was crowded with microzymes. Each inoculation was performed with a distinct pipette which had previously been roasted and cooled. The eight éprouvettes were then plugged with cotton wool, and set aside under a bell-jar. At the end of a week the first seven were found absolutely limpid and barren. The eighth was milky, and coated with a scum of bacteria.

2. The disinfected solutions contained the following proportions of permanganate: 1, ·5, ·25, ·125, ·0625, ·03125 per cent. The test-liquids inoculated with all of them remained barren, while that inoculated with the original solution became quickly turbid.

3. Proportion per cent. of the permanganate: ·125, ·0625, ·03125, ·015625, ·0079, ·0039. The last solution only, that containing ·0039 per cent. was found to have retained its infective power.

II. *Action of Chlorine on Septic Microzymes.*

Experiments with chlorine.

1. Proportions by weight of chlorine in disinfected solutions: ·0428, ·0214, ·00428, ·00214 per cent. Test-liquids inoculated all proved barren.

2. Proportions of chlorine per cent.: ·008, ·004, ·0016, ·0008, ·0004. All the test-liquids remained barren except the last, inoculated with a solution which contained ·0004 per cent. of the gas.

III.—*Action of Sulphur Dioxide on Septic Microzymes.*

Experiments with sulphur dioxide.

1. Proportion of SO_2 per cent. in disinfected solutions: ·528, ·0528, ·0264, ·00528, ·00264. Of the test-liquids inoculated from these solutions, one only, that inoculated with the solution containing ·528 per cent. of SO_2, remained barren.

2. Proportion of SO_2 per cent. ·495, ·248, ·123. All the test-liquids remained barren.

3. Proportion of SO_2 per cent. ·552, ·776, ·194. All the test-liquids proved barren.

IV.—*Action of Carbolic Acid on Septic Microzymes.*

Experiments with carbolic acid.

1. Proportion of carbolic acid per cent. in disinfected solutions; 4, 3, 2, 1, ·5, ·25. Test-liquids all remained barren except that inoculated with solution containing ·25 per cent. of the acid.

2. Proportion of carbolic acid per cent. 2, 1, ·5, ·25, ·125. Test-liquids inoculated with the first two proved barren, those with the last three, fertile.

3. Proportion of carbolic acid per cent. 1, ·5, ·25, ·125, ·0625. Test-liquids inoculated with first two proved barren; with last three, fertile.

Summary of results.

The somewhat unexpected results of these four series of experiments may be thus briefly summarised: the microzymes which swarm in Cohn's solution are completely deprived of reproductive power by potassic permanganate, when present in the proportion of ·007 per cent. or more; by chlorine, when present in the proportion of ·0008 per cent. or more; by sulphur dioxide, when present in the proportion of ·123 per cent. or

more; by carbolic acid, when present in the proportion of 1 per cent. or more. The time during which the microzymes were exposed to the action of the disinfectant did not appear to matter; intermixture having been thoroughly accomplished, the work was done.

Apparent discrepancy between antiseptic and disinfectant power.

The striking *primâ facie* discrepancy between these figures and those obtained in the series of experiments performed with vaccine lymph, would have led to the abandonment of the inquiry, had not the results of Davaine's experiments on the virus of charbon (p. 22.) awakened the suspicion that the discrepancy was more apparent than real. It is noteworthy that the difference was greatest in the case of chlorine and potassic permanganate; least in the case of carbolic acid; and that the figures obtained with the virus of glanders and of infective inflammation, were less widely removed from those representing the antiseptic power of the four agents, than those obtained in the case of vaccine.

Attempt to elucidate the nature of this discrepancy.

There are two alternative explanations possible: it may be that the particles of contagium differ so essentially from one another and from the germs of septic microzymes in their susceptibility to adverse conditions, that no common prospect, whether of destruction or survival, can be held out to all of them alike; on the other hand, it is possible that the particles are all equally liable to perish when brought into contact with the same disinfectants; and that the discrepancy observed is entirely due to differences in the medium in which the particles may happen to float. The probability of the latter explanation is enhanced by the reflexion that septic microzymes, which are admittedly of one kind, vary widely in the degree of their resistance to destructive agencies, according to their physical condition and environment.*

In order to obtain some evidence on which to found a judgment between these two conflicting views, the following experiments were carried out. It was obviously impossible to vary the nature of the medium in which the particles of vaccine virus are suspended—a medium strongly alkaline, and loaded with coagulable principles,—owing chiefly to the small quantity of material available for experiment. So that, in the first place, an attempt was made to alter the constitution of the medium containing septic microzymes, and by bringing it more nearly into relation with the albuminoid matrix of vaccine lymph, to ascertain whether changes made in this direction were attended by any corresponding change in the susceptibility of the septic germs to the action of chlorine and permanganate.

Experiments with septic microzymes.

I. Two solutions containing active microzymes in abundance, were prepared as follows: (*a*) by mixing 2 c.c. of turbid Cohn with 18 c.c. of water; (*b*) by mixing 2 c.c. of turbid Cohn with 18 c.c. of ovalbumin. The former was neutral, the latter feebly alkaline. Each solution was divided into three parts, and potassic permanganate was introduced in the following proportions:

1*a* and 1*b*	received	·0125	per cent.
2*a* „ 2*b*	„	·00625	„
3*a* „ 3*b*	„	·003125	„

The solutions were all shaken and put under a bell-jar. Eight éprouvettes, charged with sterilised test-liquid, having been prepared, six were inoculated from the above six solutions; the seventh received a drop of (*a*); the eighth, a drop of (*b*). After a week had elapsed, it was found that the test-liquids inoculated from the three disinfected solutions which

* No particular evidence in support of this assertion need be given, for nearly all the facts adduced during the recent controversy on spontaneous generation are illustrative of its truth.

contained no albumen, were barren; while the other five were turbid and swarmed with microzymes.

Another experiment of a similar kind showed that the presence of ·025 per cent. of permanganate failed to destroy the reproductive power of septic microzymes suspended in an albuminous medium.

II. An experiment of the same kind was performed with chlorine. It was found that proportions of ·016, ·008, and ·004 per cent. of the gas proved fatal to septic microzymes in a watery medium, and harmless to the same microzymes in an albuminous one.

Another experiment was carried out with larger proportions of the disinfectant: it was found that ·1954 per cent. succeeded in destroying the septic germs both in the albuminous and in the aqueous media, while ·065, ·033, and ·016 per cent. succeeded in aqueous and failed in albuminous solutions. After the chlorine had been incorporated with the solutions they were all tested with iodide of potassium and starch; free chlorine was found in *all* the aqueous solutions, but only in the first of the albuminous ones, that in which its antiseptic power was alone manifested.

The results of the above experiments are strongly in favour of the view that the difference between septic germs and the particles of vaccine virus, as regards their susceptibility to chlorine and permanganate, depends chiefly, if not entirely, on the difference of the media in the two cases. Similar trials made with sulphur dioxide and carbolic acid yielded results of another order, as will be seen from the following account of them.

III. Septic microzymes suspended in aqueous and albuminous media were exposed to the action of carbolic acid in proportions of ·5, 1, and 2 per cent. The acid was found to sterilise both the aqueous and the albuminous solutions in proportions of 1 and 2 per cent., and to fail in both alike when present in the proportion of only ·5 per cent.

IV. Similar experiments with sulphur dioxide showed that when present in proportions of 1·5, ·77, and ·194 per cent., the gas destroyed the reproductive capacity of septic microzymes both in albuminous and aqueous media.

It thus appears that the action of potassic permanganate and chlorine on septic germs is interfered with by the presence of albumen in the medium in which the germs float; and that the protective power of albumen is less marked, if it exist at all, in the case of sulphur dioxide and carbolic acid.

Experiments with virus of infective inflammation.

An endeavour was now made to corroborate the inference from these experiments by following another line of inquiry. Although, as has been stated before, it was not found possible to modify the medium in which the particles of vaccine are suspended, the same difficulty was not presented by the virus of infective inflammation. Accordingly a sufficiency of viscid matter from the peritoneum of an infected guinea-pig having been procured, it was divided into two equal parts; one was directly exposed to the action of potassic permanganate, the other was freed from all soluble admixture by repeated washing and decantation.* The latter liquid ultimately consisted of nearly pure saline solution in which flocculi of exudation were suspended; under the microscope these flocculi were seen to consist of corpuscular elements, studded with minute refracting particles (*Micrococci?*). This latter liquid was mixed with permanganate in the same proportions as the former one; the result of the series of inoculations performed with the two kinds of virus is given in the following table.

* This method is the same as that adopted in the case of glanders virus, and described on p. 24.

Series.	No. of Animal.	Weight in Grammes.	Date of Inoculation.	Material Inoculated.	Dose.	Proportion of Disinfectant in the Material Inoculated.	Interval of Time between Inoculation and Death.	Post-mortem Appearances, and Remarks.
X.	27	462	October 30	Washed virus (flakes of exudation suspended in saline solution) diluted with equal volume of water.	$3\frac{1}{2}$ m	0	5 days	Infective peritonitis; viscid, colourless exudation; surface of liver smeared with yellowish flaky lymph. No pleurisy or pericarditis. Changes at site of inoculation inconsiderable.
	28	532	Do.	Same washed virus with equal volume of permanganate solution.	$3\frac{1}{2}$ m	·05 per cent. of permanganate.	- - -	No symptoms. Used for another experiment on January 14.
	29	510	Do.	Ditto - - - -	$3\frac{1}{2}$ m	·025 per cent. of permanganate.	- - -	Ditto.
	30	470	November 4	Same virus, but not washed; highly viscid and coagulable. Diluted with equal volume of saline solution.	$3\frac{1}{2}$ m	0	4 days	Local changes as in 27. Peritonitis with viscid exudation and abundant flaky lymph. Double pleurisy and pericarditis.
	31	610	Do.	Same virus, not washed, mixed with equal volume of permanganate solution.	$3\frac{1}{2}$ m	·05 per cent. of permanganate.	6 days	Peritonitis, left pleurisy, and pericarditis. Nature of exudation same as in 27 and 30.
	32	508	Do.	Ditto - - - -	$3\frac{1}{2}$ m	·025 per cent. of permanganate.	3 days	Peritonitis with scanty reddish exudation. No pericarditis or pleurisy.

The result of this very demonstrative experiment, when taken in conjunction with that of Davaine's experiments on charbon virus suspended in a watery liquid (p. 22), places the protective influence of the medium above all question, at least as regards potassic permanganate. The following two series of experiments were designed to ascertain whether the disinfectant activity of chlorine was capable of being interfered with by alkalinity of the virulent medium, or by the presence in it of albuminous matter.

Series.	No. of Animal.	Weight in Grammes.	Date of Inoculation.	Material Inoculated.	Dose.	Proportion of Disinfectant in the Material Inoculated.	Interval of Time between Inoculation and Death.	Post-mortem Appearances, and Remarks.
XI.	33	300	February 11	Virus 5 parts; 10 per cent. solution of sodic carbonate 1 part. Strongly alkaline. The virus was the same as that employed in series III.	5 m	0	16 hours	Same appearances as in No. 7.
	34	560	Do.	Virus 4 parts; saline solution 1 part; chlorine water 1 part. Distinctly acid; traces of pure chlorine can just be detected by iodide of potassium and starch.	5 m	·0544 per cent. chlorine.	- - -	No symptoms. In perfect health on March 16.
	35	888	Do.	Virus 4 parts; 10 per cent. solution of sodic carbonate, 1 part; chlorine water, 1 part. Strongly alkaline; free chlorine present in abundance as shewn by potassic iodide and starch.	5 m	·0544 per cent. chlorine.	- - -	Ditto.
XII.	36	645	February 16	Virus, 1 part; saline solution, 3 parts. Neutral. Same virus as in series XI.	5 m	0	36 hours	Same appearances as in No. 33.
	37	428	Do.	Virus, 1 part; saline solution, 2 parts; chlorine water, 1 part. Contains free chlorine in abundance.	5 m	·0793 per cent. chlorine.	- - -	No symptoms. Quite well on March 16.
	38	390	Do.	Virus, 1 part; ovalbumin, 2 parts; chlorine water, 1 part. No free chlorine to be detected.	5 m	·0793 per cent. chlorine.	24 hours	Same appearances as in No. 33.

The above results tend to the conclusion that a high degree of alkalinity of the virulent medium does not impair the disinfectant power of chlorine, while the presence of a certain proportion of albumen nullifies its activity.

To sum up: the evidence of the foregoing experiments, such as it is, points in one direction, and lends support to the view that such quantitative differences as seem at first sight to exist between the disinfectant action of chlorine and potassic permanganate on the various contagia on the one hand, and on the germinal matter of septic microzymes on the other—and those differences are very marked—are chiefly, if not entirely, due to differences in the nature of the medium in which the particles, whether of septic or of contagious matter, are suspended. Carbolic acid and sulphur dioxide seem to be less at the mercy of the medium in which they are required to operate; accordingly the quantitative difference between the action of carbolic acid on the contagia, and its action on septic microzymes, is trifling when compared with that exhibited by chlorine and the permanganate.

Hence it follows that the destructive action of a substance on the reproductive power of septic microzymes does really appear to afford some clue to its strictly disinfectant properties; but that, in order to make antiseptic a measure of disinfectant energy, it is essential to follow the method of inquiry recommended above, to understand "antiseptic" as synonymous with "fatal to the reproductive power of microzymes," and to eliminate chemical phenomena of putrefaction as altogether foreign to the subject. Further, it must never be forgotten that the nature of the medium in which the particles, whether septic or contagious, are embedded or suspended, exerts a modifying influence of the most striking kind on the susceptibility of the particles themselves to disinfectant agents.

Principal inferences from the above research embodied in the form of propositions.

It may be well, in conclusion, to embody the principal inferences which seem to flow from the results of the foregoing investigation in a series of propositions. The basis of induction furnished by it is, of course, a relatively narrow one; but, though narrow, it appears to be more secure than that which has hitherto been built upon.*

1. Evidence has been adduced to show that carbolic acid, sulphur dioxide, potassic permanganate, and chlorine, are all of them endowed with true disinfectant properties, though in very various degrees.

2. It is essential to bear in mind that antiseptic is not synonymous with disinfectant power, though, as regards the four agents enumerated above, the one is, in a certain limited sense, commensurate with the other.

3. The effectual disinfectant operation of chlorine and potassic permanganate appears to depend far more on the nature of the medium through which the particles of infective matter are distributed, than on the specific character of the particles themselves.

4. When either of these agents is used to disinfect a virulent liquid containing much organic matter, or any compounds capable of uniting with chlorine, or of decomposing the permanganate, there is no security for the effectual fulfilment of disinfection short of the presence of free chlorine or undecomposed permanganate in the liquid after all chemical action has had time to subside.

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* These propositions are simply meant to help the reader in gaining a succinct view of the more practical bearings of the foregoing research; the evidence on which some of them rest is obviously too limited in *quantity*, though of the right *kind*, to allow of their laying any claim to finality.

5. A virulent liquid cannot be regarded as certainly and completely disinfected by sulphur dioxide unless it has been rendered permanently and strongly acid. The greater solubility of this agent renders it preferable, *cæteris paribus*, to chlorine and carbolic acid, for the disinfection of liquid media.

6. No virulent liquid can be considered disinfected by carbolic acid unless it contain at least 2 per cent. by weight of the pure acid.

7. When disinfectants are mixed with a liquid, it is important to be sure that they are thoroughly incorporated with it; that no solid matters capable of shielding contagium from immediate contact with its destroyer be overlooked.

8. Aerial disinfection, as commonly practised in the sick-room, is either useless or positively objectionable, owing to the false sense of security it is calculated to produce. To make the air of a room smell strongly of carbolic acid by scattering carbolic powder about the floor, or of chlorine, by placing a tray of chloride of lime in a corner, is, so far as the destruction of specific contagia is concerned, an utterly futile proceeding.

9. When aerial disinfection is resorted to, the probability that the virulent particles are shielded by an envelope of dried albuminous matter, should always be held before the mind. Chlorine and sulphur dioxide are, both of them, suitable agents for the purpose; the latter seems decidedly to be the more effectual of the two. The use of carbolic vapour should be abandoned, owing to the relative feebleness and uncertainty of its action. Whether chlorine or sulphur dioxide be chosen, it is desirable that the space to be disinfected should be kept saturated with the gas for a certain time, not less than an hour; and this in the absence of such gaseous compounds as might combine with or decompose the disinfectant, and so far impair its energy.

10. When the thorough disinfection of a mass of solid or liquid matter, through which a contagium is disseminated, is impracticable,* we should guard against giving a false security by the inadequate employment of artificial means. It is probable that all contagia disappear sooner or later under the influence of air and moisture, and that the absence of these influences may act as a preservative. When, therefore, we cannot advantageously or effectually supersede the natural process of decay, we must be sure that we do not hamper it by the injudicious use of antiseptics.

11. Dry heat, when it can be applied, is probably the most efficient of all disinfectants. But, in the first place, we must be sure that the desired temperature is actually reached by every particle of matter included in the heated space;† secondly, length of exposure and degree of heat should be regarded as mutually compensatory factors, within certain limits.

The above statements are not so discouraging as they may appear at the first glance to our reliance upon artificial disinfection. If we believe that all contagia are generated, like those of small-pox and scarlet fever, in the infected organism, and there only, the out-look is a hopeful one. We might even anticipate an approach to the *perfect* fulfilment of the

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* As an example, we may take the accumulation of manure and litter from a number of animals suffering from cattle-plague.

† This point has been investigated, and its importance established, by Dr. Ransome.

App. No. 6.
On Disinfectants, by Dr. Baxter.

work of disinfection, by subjecting all matters, immediately after their removal from the affected person, and before any dilution or admixture, to the full influence of one or other among the destructive agencies at our command. On the other hand, if the contagium of any disease is capable of being generated *de novo* outside the body (pythogenic origin of enteric fever, typhus created by overcrowding) such contagium can hardly be eradicated by any method of artificial disinfection. For cases of the latter kind, the opening words of the memorandum previously referred to, furnish the only solution. "It is to cleanliness, ventilation, "and drainage, and the use of perfectly pure drinking-water, that "populations ought mainly to look for safety against nuisance and "infection. Artificial disinfectants cannot properly supply the place "of these essentials; for, except in a small and peculiar class of cases, "they are of temporary and imperfect usefulness."

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